



DIRECTOR'S REPORT

————— *to the* —————
National Advisory Council on Drug Abuse
————— *May 2015* —————

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Director
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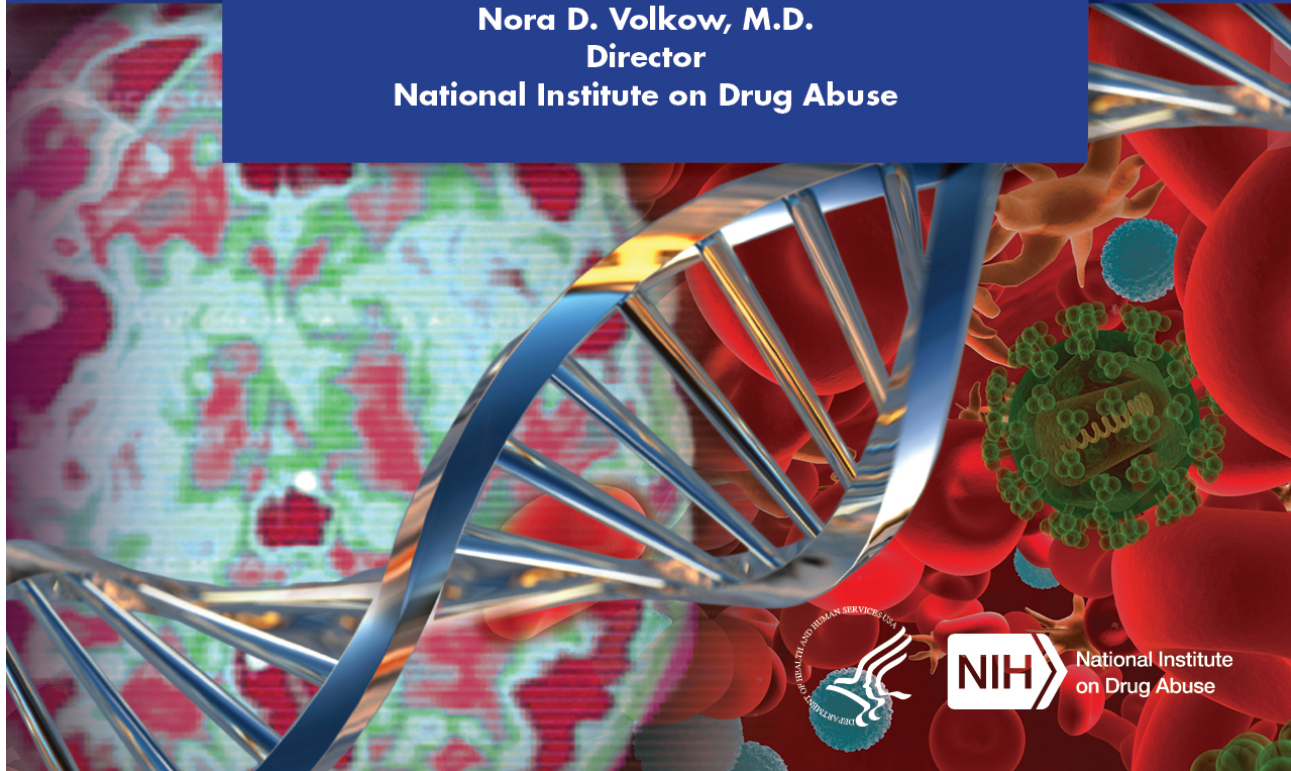


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** These sections contain select information. More comprehensive information will be posted in the [May 2015 Staff Report to the Director](#).*

RESEARCH HIGHLIGHTS

DIVISION OF BASIC NEUROSCIENCE AND BEHAVIORAL RESEARCH (DBNBR)

[Visualizing Hypothalamic Network Dynamics For Appetitive and Consummatory Behaviors](#)

Jennings JH, Ung RL, Resendez SL, Stamatakis AM, Taylor JG, Huang J, Veleta K, Kantak PA, Aita M, Shilling-Scriver K, Ramakrishnan C, Deisseroth K, Otte S, Stuber GD. *Cell* 2015; 160(3): 516-527.

Optimally orchestrating complex behavioral states, such as the pursuit and consumption of food, is critical for an organism's survival. The lateral hypothalamus (LH) is a neuroanatomical region essential for appetitive and consummatory behaviors, but whether individual neurons within the LH differentially contribute to these interconnected processes is unknown. Here, the authors show that selective optogenetic stimulation of a molecularly defined subset of LH GABAergic (Vgat-expressing) neurons enhances both appetitive and consummatory behaviors, whereas genetic ablation of these neurons reduced these phenotypes. Furthermore, this targeted LH subpopulation is distinct from cells containing the feeding-related neuropeptides, melanin-concentrating hormone (MCH), and orexin (Orx). Employing in vivo calcium imaging in freely behaving mice to record activity dynamics from hundreds of cells, the authors identified individual LH GABAergic neurons that preferentially encode aspects of either appetitive or consummatory behaviors, but rarely both. These tightly regulated, yet highly intertwined, behavioral processes are thus dissociable at the cellular level.

[Integrative Analysis of 111 Reference Human Epigenomes](#) Roadmap Epigenomics Consortium, Kundaje A, Meuleman W, Ernst J, Bilenky M, Yen A, Heravi-Moussavi A, Kheradpour P, Zhang Z, Wang J, Ziller MJ, Amin V, Whitaker JW, Schultz MD, Ward LD, Sarkar A, Quon G, Sandstrom RS, Eaton ML, Wu Y-C, Pfenning AR, Wang X, Claussnitzer M, Liu Y, Coarfa C, Harris RA, Shores N, Epstein CB, Gjoneska E, Leung D, Xie W, Hawkins RD, Lister R, Hong C, Gascard P, Mungall AJ, Moore R, Chuah E, Tam A, Canfield TK, Hansen RS, Kaul R, Sabo PJ, Bansal MS, Carles A, Dixon JR, Farh K-H, Feizi S, Karlic R, Kim A-R, Kulkarni A, Li D, Lowdon R, Elliott G, Mercer TR, Neph SJ, Onuchic V, Polak P, Rajagopal N, Ray P, Sallari RC, Siebenthal KT, Sinnott-Armstrong NA, Stevens M, Thurman RE, Wu J, Zhang B, Zhou X, Beaudet AE, Boyer LA, De Jager PL, Farnham PJ, Fisher SJ, Haussler D, Jones SJM, Li W, Marra MA, McManus MT, Sunyaev S, Thomson JA, Tlsty TD, Tsai L-H, Wang W, Waterland RA, Zhang MQ, Chadwick LH, Bernstein BE, Costello JF, Ecker JR, Hirst M, Meissner A, Milosavljevic A, Ren B, Stamatoyannopoulos JA, Wang T, Kellis M. *Nature* 2015; 518(7539): 317-330.

The reference human genome sequence set the stage for studies of genetic variation and its association with human disease, but epigenomic studies lack a similar reference. To address this need, the NIH Roadmap Epigenomics Consortium generated the largest collection so far of human epigenomes for primary cells and tissues. Here the authors describe the integrative analysis of 111 reference human epigenomes generated as part of the programme, profiled for histone modification patterns, DNA accessibility, DNA methylation and RNA expression. The authors establish global maps of regulatory elements, define regulatory modules of coordinated activity, and their likely activators and repressors. They show that disease- and trait-associated genetic variants are enriched in tissue-specific epigenomic marks, revealing biologically relevant cell types for diverse human traits, and providing a resource for interpreting the molecular basis of human disease. These results

demonstrate the central role of epigenomic information for understanding gene regulation, cellular differentiation and human disease.

Effects of Fatty Acid Amide Hydrolase (FAAH) Inhibitors in Non-Human Primate Models of Nicotine Reward and Relapse

Justinova Z, Panlilio LV, Moreno-Sanz G, Redhi GH, Auber A, Secci ME, Mascia P, Bandiera T, Armirotti A, Bertorelli R, Chefer SI, Barnes C, Yasar S, Piomelli D, Goldberg SR. *Neuropsychopharmacology*. 2015 Mar 10. [Epub ahead of print].

Inhibition of the enzyme fatty acid amide hydrolase (FAAH) counteracts reward-related effects of nicotine in rats, but has not been tested for this purpose in non-human primates. Therefore, the authors studied the effects of the first- and second-generation O-arylcarbamate-based FAAH inhibitors, URB597 (cyclohexyl carbamic acid 3'-carbamoyl-3-yl ester) and URB694 (6-hydroxy-[1,1'-biphenyl]-3-yl-cyclohexylcarbamate), in squirrel monkeys. Both FAAH inhibitors: 1) blocked FAAH activity in brain and liver, increasing levels of endogenous ligands for cannabinoid and alpha-type peroxisome proliferator-activated (PPAR- α) receptors; 2) shifted nicotine self-administration dose-response functions in a manner consistent with reduced nicotine reward; 3) blocked reinstatement of nicotine seeking induced by re-exposure to either nicotine priming or nicotine-associated cues; and 4) had no effect on cocaine or food self-administration. The effects of FAAH inhibition on nicotine self-administration and nicotine priming-induced reinstatement were reversed by the PPAR- α antagonist, MK886. Unlike URB597, which was not self-administered by monkeys in an earlier study, URB694 was self-administered at a moderate rate. URB694 self-administration was blocked by pretreatment with an antagonist for either PPAR- α (MK886) or cannabinoid CB₁ receptors (rimonabant). In additional experiments in rats, URB694 was devoid of THC-like or nicotine-like interoceptive effects under drug-discrimination procedures, and neither FAAH inhibitor induced dopamine release in the nucleus accumbens shell-consistent with their lack of robust reinforcing effects in monkeys. Overall, both URB597 and URB694 show promise for the initialization and maintenance of smoking cessation, due to their ability to block the rewarding effects of nicotine and prevent nicotine priming-induced and cue-induced reinstatement.

Optogenetic Excitation Of Central Amygdala Amplifies and Narrows Incentive Motivation To Pursue One Reward Above Another Robinson MJF, Warlow SM, Berridge KC. *J Neurosci* 2014; 34(50): 16567-16580.

Choosing one reward above another is important for achieving adaptive life goals. Yet hijacked into excessive intensity in disorders such as addiction, single-minded pursuit becomes maladaptive. Here, the authors report that optogenetic channelrhodopsin stimulation of neurons in central nucleus of amygdala (CeA), paired with earning a particular sucrose reward in rats, amplified and narrowed incentive motivation to that single reward target. Therefore, CeA rats chose and intensely pursued only the laser-paired sucrose reward while ignoring an equally good sucrose alternative. In contrast, reward-paired stimulation of basolateral amygdala did not hijack choice. In a separate measure of incentive motivation, CeA stimulation also increased the progressive ratio breakpoint or level of effort exerted to obtain sucrose reward. However, CeA stimulation by itself failed to support behavioral self-stimulation in the absence of any paired external food reward, suggesting that CeA photo-excitation specifically transformed the value of its external reward (rather than adding an internal reinforcement state). Nor did CeA stimulation by itself induce any aversive state that motivated escape. Finally, CeA stimulation also failed to enhance 'liking' reactions elicited by sucrose taste and did not simply increase the general motivation to eat. This pattern suggests that

CeA photo-excitation specifically enhances and narrows incentive motivation to pursue an associated external reward at the expense of another comparable reward.

Large-Scale Topology and The Default Mode Network In The Mouse Connectome Stafford JM, Jarrett BR, Miranda-Dominguez O, Mills BD, Cain N, Mihalas S, Lahvis GP, Lattal KM, Mitchell SH, David SV, Fryer JD, Nigg JT, Fair DA. Proc Natl Acad Sci U S A 2014; 111(52): 18745-18750.

Noninvasive functional imaging holds great promise for serving as a translational bridge between human and animal models of various neurological and psychiatric disorders. However, despite a depth of knowledge of the cellular and molecular underpinnings of atypical processes in mouse models, little is known about the large-scale functional architecture measured by functional brain imaging, limiting translation to human conditions. Here, the authors provide a robust processing pipeline to generate high-resolution, whole-brain resting-state functional connectivity MRI (rs-fcMRI) images in the mouse. Using a mesoscale structural connectome (i.e., an anterograde tracer mapping of axonal projections across the mouse CNS), the authors show that rs-fcMRI in the mouse has strong structural underpinnings, validating our procedures. They next directly show that large-scale network properties previously identified in primates are present in rodents, although they differ in several ways. Last, they examine the existence of the so-called default mode network (DMN)--a distributed functional brain system identified in primates as being highly important for social cognition and overall brain function and atypically functionally connected across a multitude of disorders. The authors show the presence of a potential DMN in the mouse brain both structurally and functionally. Together, these studies confirm the presence of basic network properties and functional networks of high translational importance in structural and functional systems in the mouse brain. This work clears the way for an important bridge measurement between human and rodent models, enabling us to make stronger conclusions about how regionally specific cellular and molecular manipulations in mice relate back to humans.

DIVISION OF CLINICAL NEUROSCIENCE AND BEHAVIORAL RESEARCH (DCNBR)

Neural Substrates of Approach-Avoidance Conflict Decision-Making Aupperle RL, Melrose AJ, Francisco A, Paulus MP, Stein MB. Human Brain Mapping. 2015; 36(2):449–462.

Animal approach-avoidance conflict paradigms have been used extensively to operationalize anxiety, quantify the effects of anxiolytic agents, and probe the neural basis of fear and anxiety. Results from human neuroimaging studies support that a frontal-striatal-amygdala neural circuitry is important for approach-avoidance learning. However, the neural basis of decision-making is much less clear in this context. Thus, the authors combined a recently developed human approach-avoidance paradigm with functional magnetic resonance imaging (fMRI) to identify neural substrates underlying approach-avoidance conflict decision-making. Fifteen healthy adults completed the approach-avoidance conflict (AAC) paradigm during fMRI. Analyses of variance were used to compare conflict to nonconflict (avoid-threat and approach-reward) conditions and to compare level of reward points offered during the decision phase. Trial-by-trial amplitude modulation analyses were used to delineate brain areas underlying decision-making in the context of approach/avoidance behavior. Conflict trials as compared to the nonconflict trials elicited greater activation within bilateral anterior cingulate cortex, anterior insula, and caudate, as well as right dorsolateral prefrontal cortex (PFC). Right caudate and lateral PFC activation was modulated by

level of reward offered. Individuals who showed greater caudate activation exhibited less approach behavior. On a trial-by-trial basis, greater right lateral PFC activation related to less approach behavior. Taken together, results suggest that the degree of activation within prefrontal-striatal-insula circuitry determines the degree of approach versus avoidance decision-making. Moreover, the degree of caudate and lateral PFC activation related to individual differences in approach-avoidance decision-making. Therefore, the approach-avoidance conflict paradigm is ideally suited to probe anxiety-related processing differences during approach-avoidance decision-making.

[Insula-Dorsal Anterior Cingulate Cortex Coupling is Associated with Enhanced Brain Reactivity to Smoking Cues](#)

Janes AC, Farmer S, Peechatka AL, Frederick BB, Lukas SE. *Neuropsychopharmacology*. 2015 Jan. [Epub ahead of print].

The insula plays a critical role in maintaining nicotine dependence and reactivity to smoking cues. More broadly, the insula and the dorsal anterior cingulate cortex (dACC) are key nodes of the salience network (SN), which integrates internal and extrapersonal information to guide behavior. Thus, insula-dACC interactions may be integral in processing salient information such as smoking cues that facilitate continued nicotine use. The authors evaluated functional magnetic resonance imaging (fMRI) data from nicotine-dependent participants during rest, and again when they viewed smoking-related images. Greater insula-dACC coupling at rest was significantly correlated with enhanced smoking cue-reactivity in brain areas associated with attention and motor preparation, including the visual cortex, right ventral lateral prefrontal cortex, and the dorsal striatum. In an independent cohort, the authors found that insula-dACC connectivity was stable over 1-h delay and was not influenced by changes in subjective craving or expired carbon monoxide, suggesting that connectivity strength between these regions may be a trait associated with heightened cue-reactivity. Finally, they also showed that insula reactivity to smoking cues correlates with a rise in cue-reactivity throughout the entire SN, indicating that the insula's role in smoking cue-reactivity is not functionally independent, and may actually represent the engagement of the entire SN. Collectively, these data provide a more network-level understanding of the insula's role in nicotine dependence and shows a relationship between inherent brain organization and smoking cue-reactivity.

[Distinct Brain Systems Mediate the Effects of Nociceptive Input and Self-regulation on Pain](#)

Woo CW, Roy M, Buhle JT, Wager TD. *PLoS Biol*. 2015 Jan 6; 13(1): e1002036. Cognitive self-regulation can strongly modulate pain and emotion. However, it is unclear whether self-regulation primarily influences primary nociceptive and affective processes or evaluative ones. In this study, participants engaged in self-regulation to increase or decrease pain while experiencing multiple levels of painful heat during functional magnetic resonance imaging (fMRI) imaging. Both heat intensity and self-regulation strongly influenced reported pain, but they did so via two distinct brain pathways. The effects of stimulus intensity were mediated by the neurologic pain signature (NPS), an a priori distributed brain network shown to predict physical pain with over 90% sensitivity and specificity across four studies. Self-regulation did not influence NPS responses; instead, its effects were mediated through functional connections between the nucleus accumbens and ventromedial prefrontal cortex. This pathway was unresponsive to noxious input, and has been broadly implicated in valuation, emotional appraisal, and functional outcomes in pain and other types of affective processes. These findings provide evidence that pain reports are associated with two dissociable functional systems: nociceptive/affective aspects mediated by the NPS, and evaluative/functional aspects mediated by a fronto-striatal system.

Predisposition to and Effects of Methamphetamine Use on the Adolescent Brain Lyoo IK, Yoon S, Kim TS, Lim SM, Choi Y, Kim JE, Hwang J, Jeong HS, Cho HB, Chung YA, Renshaw PF. *Mol Psychiatry*. 2015 Feb 10. doi: 10.1038/mp.2014.191. [Epub ahead of print]. Adolescence is a period of heightened vulnerability both to addictive behaviors and drug-induced brain damage. Yet, only limited information exists on the brain mechanisms underlying these adolescent-specific characteristics. Moreover, distinctions in brain correlates between predisposition to drug use and effects of drugs in adolescents are unclear. Using cortical thickness and diffusion tensor image analyses, the authors found greater and more widespread gray and white matter alterations, particularly affecting the frontostriatal system, in adolescent methamphetamine (MA) users compared with adult users. Among adolescent-specific gray matter alterations related to MA use, smaller cortical thickness in the orbitofrontal cortex was associated with family history of drug use. These findings highlight that the adolescent brain, which undergoes active myelination and maturation, is more vulnerable to MA-related alterations than the adult brain. Furthermore, MA-use-related executive dysfunction was greater in adolescent MA users than in adult users. These findings may provide explanation for the severe behavioral complications and relapses that are common in adolescent-onset drug addiction. Additionally, these results may provide insights into distinguishing the neural mechanisms that underlie the predisposition to drug addiction from effects of drugs in adolescents.

Executive Function and Cortical Thickness in Youths Prenatally Exposed to Cocaine, Alcohol and Tobacco Gautam P, Warner TD, Kan EC, Sowell ER. *Dev Cogn Neurosci*. 2015 Feb 2. pii: S1878-9293(15)00024-9.

Small and detrimental, albeit inconsistent, effects of prenatal cocaine exposure (PCE) during early childhood have been reported. The teratogenic effects of prenatal alcohol (PAE) and tobacco exposure (PTE) on neurobehavior are more firmly established than PCE. The authors tested if co-exposure to all three drugs could be related to greater differences in brain structure than exposure to cocaine alone. Participants (n=42, PCE=27; age range=14-16 years) received an executive function battery prior to a T1-weighted 3T structural MRI scan. Cortical thickness was measured using FreeSurfer (v5.1). Fetal drug exposure was quantified through maternal self-reports usage during pregnancy. Using general linear modeling, the authors found no main effects of PCE on cortical thickness, but significant main effects of PAE and PTE in superior and medial frontal regions, after co-varying for the effects of age, sex, and each drug of exposure. Significant alcohol-by-tobacco interactions and significant cocaine-by-alcohol interactions on cortical thickness in medial parietal and temporal regions were also observed. Poly-drug exposure and cognitive function also showed significant interactions with cortical thickness: lower cortical thickness was associated with better performance in PCE-exposed adolescents. Results suggest that although children with PCE have subtle brain cortical differences, these differences persist until mid-to-late adolescence.

Prenatal Tobacco Exposure and Infant Stress Reactivity: Role of Child Sex and Maternal Behavior Eiden RD, Molnar DS, Granger DA, Colder CR, Schuetze P, Huestis MA. *Dev Psychobiol*. 2015 Mar; 57(2):212-225.

This study examined the association between prenatal tobacco exposure (PTE) and infant cortisol reactivity at 9 months of infant age. Child sex and maternal parenting behavior were hypothesized moderators. The sample included 217 (148 tobacco-exposed, 69 non-exposed) mother-child dyads. Data used were obtained from pregnancy assessments, mother-infant feeding interactions at 2 months, and salivary cortisol at four time points in response to frustration at 9 months. Results

indicated a significant association between PTE and infant cortisol that was moderated by infant sex and maternal intrusiveness. That is, PTE boys had lower cortisol than control boys, but there was no association between PTE and cortisol among girls. There was a significant association between PTE and cortisol among infants of intrusive mothers, but not among infants with non-intrusive mothers. Thus, PTE was associated with cortisol hypo-reactivity such that boys and non-exposed infants experiencing high maternal intrusiveness were at greater risk.

Nicotine Concentrations with Electronic Cigarette Use: Effects of Sex and Flavor Oncken CA, Litt MD, McLaughlin LD, Burki NA. *Nicotine Tob Res.* 2015 Apr; 17(4):473-478.

This study examined overall changes in nicotine concentrations when using a popular e-cigarette and 18mg/mL nicotine e-Juice, and it further explored effects of sex and flavorings on these concentrations. The authors recruited nontreatment-seeking smokers who were willing to try e-cigarettes for 2 weeks and abstain from cigarette smoking. Subjects were randomized to either menthol tobacco or non-menthol tobacco-flavored e-cigarette use for 7-10 days, and the next week they were crossed over to the other condition. On the last day of e-cigarette use of each flavor, subjects completed a laboratory session in which they used the e-cigarette for 5min ad libitum. Nicotine concentrations were obtained 5min before and 5, 10, 15, 20, and 30min after the onset of e-cigarette use. Twenty subjects completed at least 1 monitoring session. Nicotine concentrations significantly increased from baseline to 5min by 4ng/mL at the first laboratory session ($p < .01$) and by 5.1ng/mL at the second laboratory session ($p < .01$). Combining sessions, there were no main effects of sex or preferred flavor (based on smoking history) on changes in nicotine concentrations. After adding preferred flavor, sex, and visit order to the model, there was a significant preferred flavor by sex interaction ($p < .01$), such that women who received nonpreferred flavors had lower nicotine concentrations and rated their e-cigarette as less likeable ($p < .01$). The authors found nicotine concentrations significantly increase after e-cigarette use for 5min, and flavor may impact nicotine concentrations with e-cigarette use in women.

Contingency Management Improves Smoking Cessation Treatment Outcomes among Highly Impulsive Adolescent Smokers Relative to Cognitive Behavioral Therapy Morean ME, Kong G, Camenga DR, Cavallo DA, Carroll KM, Pittman B, Krishnan-Sarin S. *Addict Behav.* 2015 Mar; 42:86-90.

Impulsive adolescents have difficulty quitting smoking. The authors examined if treatments that provide behavioral incentives for abstinence improve treatment outcomes among impulsive adolescent smokers, who have been shown to be highly sensitive to reward. They ran secondary data analyses on 64 teen smokers (mean age=16.36 [1.44]; cigarettes/day=13.97 [6.61]; 53.1% female; 90.6% Caucasian) who completed a four-week smoking cessation trial to determine whether impulsive adolescents differentially benefit from receiving cognitive behavioral therapy (CBT), contingency management (CM), or the combination of the two (CM/CBT). Indices of treatment efficacy included self-report percent days abstinent and end of treatment biochemically-confirmed 7-day point prevalence abstinence (EOT abstinence). The authors assessed self-reported impulsivity using the Brief Barratt Impulsiveness Scale. They used univariate Generalized Linear Modeling to examine main effects and interactions of impulsivity and treatment condition as predictors of self-reported abstinence, and exact logistic regression to examine EOT abstinence. CM/CBT and CM were comparably effective in promoting abstinence, so analyses were conducted comparing the efficacy of CBT to treatments with a CM component (i.e., CM and CM/CBT). CBT and deficient self-regulation predicted lower self-reported abstinence rates within the total analytic sample.

Treatments containing CM were more effective than CBT in predicting 1) self-reported abstinence among behaviorally impulsive adolescents (% days abstinent: CM 77%; CM/CBT 81%; CBT 30%) and 2) EOT point prevalence abstinence among behaviorally impulsive adolescents and adolescents with significant deficits in self-regulation. CM-based interventions may improve the low smoking cessation rates previously observed among impulsive adolescent smokers.

Adding an Internet-delivered Treatment to an Efficacious Treatment Package for Opioid Dependence Christensen DR, Landes RD, Jackson L, Marsch LA, Mancino MJ, Chopra MP, Bickel WK. *J Consult Clin Psychol.* 2014 Dec; 82(6): 964-972.

The objective of this study was to examine the benefit of adding an Internet-delivered behavior therapy to a buprenorphine medication program and voucher-based motivational incentives. A block-randomized, unblinded, parallel, 12-week treatment trial was conducted with 170 opioid-dependent adult patients (mean age = 34.3 years; 54.1% male; 95.3% White). Participants received an Internet-based community reinforcement approach intervention plus contingency management (CRA+) and buprenorphine or contingency management alone (CM-alone) plus buprenorphine. The primary outcomes, measured over the course of treatment, were longest continuous abstinence, total abstinence, and days retained in treatment. Compared to those receiving CM-alone, CRA+ recipients exhibited, on average, 9.7 total days more of abstinence (95% confidence interval [CI = 2.3, 17.2]) and had a reduced hazard of dropping out of treatment (hazard ratio = 0.47; 95% CI [0.26, 0.85]). Prior treatment for opioid dependence significantly moderated the additional improvement of CRA+ for longest continuous days of abstinence. These results provide further evidence that an Internet-based CRA+ treatment is efficacious and adds clinical benefits to a contingency management/medication based program for opioid dependence.

DIVISION OF EPIDEMIOLOGY, SERVICES AND PREVENTION RESEARCH (DESPR)

Natural Course Of Cannabis Use Disorders Farmer RF, Kosty DB, Seeley JR, Duncan SC, Lynskey MT, Rohde P, Klein DN, Lewinsohn PM. *Psychol Med.* 2015; 45(1): 63-72.

Despite its importance as a public health concern, relatively little is known about the natural course of cannabis use disorders (CUDs). The primary objective of this research was to provide descriptive data on the onset, recovery and recurrence functions of CUDs during the high-risk periods of adolescence, emerging adulthood and young adulthood based on data from a large prospective community sample. Probands (n = 816) from the Oregon Adolescent Depression Project (OADP) participated in four diagnostic assessments (T1-T4) between the ages of 16 and 30 years, during which current and past CUDs were assessed. The weighted lifetime prevalence of CUDs was 19.1% with an average onset age of 18.6 years. Although gender was not significantly related to the age of initial CUD onset, men were more likely to be diagnosed with a lifetime CUD. Of those diagnosed with a CUD episode, 81.8% eventually achieved recovery during the study period. Women achieved recovery significantly more quickly than men. The recurrence rate (27.7%) was relatively modest, and most likely to occur within the first 36 months following the offset of the first CUD episode. CUD recurrence was uncommon after 72 months of remission and recovery. CUDs are relatively common, affecting about one out of five persons in the OADP sample prior to the age of 30 years. Eventual recovery from index CUD episodes is the norm, although about 30% of those with a CUD exhibit a generally persistent pattern of problematic use extending 7 years or longer.

Genetic Predisposition To Schizophrenia Associated With Increased Use Of Cannabis Power RA, Verweij KJH, Zuhair M, Montgomery GW, Henders AK, Heath AC, Madden PAF, Medland SE, Wray NR, Martin NG. *Mol Psychiatry*. 2014; 19(11): 1201-1204.

Cannabis is the most commonly used illicit drug worldwide. With debate surrounding the legalization and control of use, investigating its health risks has become a pressing area of research. One established association is that between cannabis use and schizophrenia, a debilitating psychiatric disorder affecting ~1% of the population over their lifetime. Although considerable evidence implicates cannabis use as a component cause of schizophrenia, it remains unclear whether this is entirely due to cannabis directly raising risk of psychosis, or whether the same genes that increase psychosis risk may also increase risk of cannabis use. In a sample of 2082 healthy individuals, the authors show an association between an individual & burden of schizophrenia risk alleles and use of cannabis. This was significant both for comparing those who have ever versus never used cannabis ($P=2.6 \times 10^{-4}$), and for quantity of use within users ($P=3.0 \times 10^{-3}$). Although directly predicting only a small amount of the variance in cannabis use, these findings suggest that part of the association between schizophrenia and cannabis is due to a shared genetic etiology. This form of gene-environment correlation is an important consideration when calculating the impact of environmental risk factors, including cannabis use.

The Causes of Parent-offspring Transmission of Drug Abuse: A Swedish Population-based Study Kendler KS, Ohlsson H, Sundquist K, Sundquist J. *Psychol Med*. 2015; 45(1): 87-95.

While drug abuse (DA) is strongly familial, we still have limited knowledge about the causes of its cross-generational transmission. The authors examined DA ascertained from national registers in offspring of three family types from the Swedish population [intact ($n = 2,111,074$), not-lived-with; ($n = 165,315$, where biological parents never lived with their offspring) and step; ($n = 124,800$ offspring)], which reflected, respectively, the effects of genes + rearing, genes only and rearing only. They replicated these results in three high-risk co-relative designs. Combined across mothers and fathers, the hazard ratio (HR) for DA in offspring given DA in parents was 3.52 in intact, 2.73 in; not-lived-with; and 1.79 in stepfamilies. In 968 biological full or half-sibling pairs one of whom was reared by and the other never lived with their parent with DA, the HR for DA was greater in the reared than ;not-lived-with; child (HR 1.57). In 64 offspring pairs of a parent with DA, the HR for DA was greater in a reared biological v. step-parented non-biological child (HR 3.33). In 321 pairs of offspring of a parent with DA one of whom was a not-lived-with biological child and the second a step-parented non-biological child, the HR for DA was greater in the biological v. stepchild (HR 1.80). Both genetic and environmental factors contribute substantially to parent-offspring resemblance for DA. The general population contains informative family constellations that can complement more traditional adoption designs in clarifying the sources of parent-offspring resemblance.

Toward A Comprehensive Developmental Model Of Smoking Initiation and Nicotine Dependence Garcia-Rodriguez O, Blanco C, Wall MM, Wang S, Jin CJ, Kendler KS. *Drug Alcohol Depend*. 2014; 144: 160-169.

This study aims to identify predictors of smoking initiation and nicotine dependence (ND) to develop a comprehensive risk-factor model based on Kendler's development model for major depression. Data were drawn from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), Wave 2 ($n=34,653$). Risk factors were divided into five developmental tiers according to Kendler's model (childhood, early adolescence, late adolescence, adulthood, past-year).

Hierarchical logistic regression models were built to predict the risk of smoking initiation and the risk of ND, given initiation. The continuation ratio (CR) was tested by ordinal logistic regression to examine whether the impact of the predictors was the same on smoking initiation or ND. The final models highlighted the importance of different tiers for each outcome. The CR identified substantial differences in the predictors of smoking initiation versus ND. Childhood tier appears to be more determinant for smoking initiation while the effect of more distal tiers (i.e. childhood and early adolescence) was tempered by more proximal ones (i.e. late adolescence, adulthood and past-year) in ND, with few sex differences. The differential effect of some predictors on each outcome shows the complexity of pathways from smoking initiation to ND. While some risk factors may be shared, others impact only at one stage or have even an inverse effect. An adaptation of Kendler developmental model for major depression showed high predictive power for smoking initiation and ND.

Delinquency and Peer Acceptance In Adolescence: A Within-person Test Of Moffitt's

Hypotheses Rulison KL, Kreager DA, Osgood DW. *Dev Psychol.* 2014; 50(11): 2437-2448.

The authors tested 2 hypotheses derived from Moffitt's (1993) taxonomic theory of antisocial behavior, both of which are central to her explanation for the rise in delinquency during adolescence. They tested whether persistently delinquent individuals become more accepted by their peers during adolescence and whether individuals who abstain from delinquent behavior become less accepted. Participants were 4,359 adolescents from 14 communities in the PROSPER study, which assessed friendship networks and delinquency from 6th (M = 11.8 years) to 9th (M = 15.3 years) grade. The authors operationalized peer acceptance as number of nominations received (in degree centrality), attractiveness as a friend (adjusted in degree centrality), and network bridging potential (betweenness centrality) and tested the hypotheses with multilevel modeling. Contrary to Moffitt's hypothesis, persistently delinquent youths did not become more accepted between early and middle adolescence, and although abstainers were less accepted in early adolescence, they became more accepted over time. Results were similar for boys and girls; when differences occurred, they provided no support for Moffitt's hypotheses for boys and were opposite of her hypotheses for girls. Sensitivity analyses in which alternative strategies and additional data were used to identify persistently delinquent adolescents produced similar results. The authors explore the implications of these results for Moffitt's assertions that social mimicry of persistently antisocial adolescents leads to increases in delinquency and that social isolation leads to abstention.

Neighborhood Poverty and Allostatic Load In African American Youth Brody GH, Lei M-K,

Chen E, Miller GE. *Pediatrics.* 2014; 134(5): e1362-1368.

This study was designed to determine whether living in a neighborhood in which poverty levels increase across adolescence is associated with heightened levels of allostatic load (AL), a biological composite reflecting cardio metabolic risk. The researchers also sought to determine whether receipt of emotional support could ameliorate the effects of increases in neighborhood poverty on AL. Neighborhood concentrations of poverty were obtained from the Census Bureau for 420 African American youth living in rural Georgia when they were 11 and 19 years of age. AL was measured at age 19 by using established protocols for children and adolescents. When youth were 18, caregivers reported parental emotional support and youth assessed receipt of peer and mentor emotional support. Covariates included family poverty status at ages 11 and 19, family financial stress, parental employment status, youth stress, and youths' unhealthful behaviors. Youth who lived in neighborhoods in which poverty levels increased from ages 11 to 19 evinced the highest

levels of AL even after accounting for the individual-level covariates. The association of increasing neighborhood poverty across adolescence with AL was not significant for youth who received high emotional support. This study is the first to show an association between AL and residence in a neighborhood that increases in poverty. It also highlights the benefits of supportive relationships in ameliorating this association.

Couple-Based HIV Counseling And Testing: A Risk Reduction Intervention For US Drug-Involved Women And Their Primary Male Partners McMahan JM, Pouget ER, Tortu S, Volpe EM, Torres L, Rodriguez W. *Prev Sci.* 2014.

To help reduce the elevated risk of acquiring HIV for African-American and Latina women drug users in primary heterosexual relationships, the authors developed a brief couple-based HIV counseling and testing prevention intervention. The intervention was based on an integrated HIV risk behavior theory that incorporated elements of social exchange theory, the theory of gender and power, the stages-of-change model, and the information-motivation-behavior skills model. In this article, the authors describe the development, content, and format of the couple-based HIV testing and counseling intervention, and its delivery to 110 couples (220 individuals) in a randomized effectiveness trial, the Harlem River Couples Project, conducted in New York City from 2005 to 2007. Components of the couple-based intervention included a personalized dyadic action plan based on the couples' risk profile and interactive exercises designed to help build interpersonal communication skills, and facilitated discussion of social norms regarding gender roles. The couple-based HIV testing and counseling intervention significantly reduced women's overall HIV risk compared to a standard-of-care individual HIV testing and counseling intervention. Experiences and perceptions of the intervention were positive among both clients and interventionists. The study was the first to demonstrate the effectiveness and feasibility of delivering a brief couple-based HIV counseling and testing intervention to reduce risk among drug-using heterosexual couples in high HIV prevalent urban communities in the USA. The intervention can be expanded to include new HIV prevention strategies, such as pre-exposure prophylaxis. Further research is needed to evaluate cost-effectiveness and implementation of the intervention in clinical settings.

Effects Of Multidimensional Treatment Foster Care On Psychotic Symptoms In Girls Poulton R, Van Ryzin MJ, Harold GT, Chamberlain P, Fowler D, Cannon M, Arseneault L, Leve LD. *J Am Acad Child Adolesc Psychiatry.* 2014; 53(12): 1279-1287.

Neurodevelopmental theories of psychosis highlight the potential benefits of early intervention, prevention, and/or preemption. How early intervention should take place has not been established, nor whether interventions based on social learning principles can have preemptive effects. The objective was to test whether a comprehensive psychosocial intervention can significantly alter psychotic symptom trajectories during adolescence—a period of heightened risk for a wide range of psychopathology. This study was a randomized controlled trial (RCT) of Multidimensional Treatment Foster Care (MTFC) for delinquent adolescent girls. Assessment of psychotic symptoms took place at baseline and then 6, 12, 18, and 24 months post-baseline using a standardized self-report instrument (Brief Symptom Inventory). A second source of information about psychotic symptoms was obtained at baseline or 12 months, and again at 24 months using a structured diagnostic interview (the Diagnostic Interview Schedule for Children [DISC]). Significant benefits for MTFC over treatment as usual for psychosis symptoms were observed over a 24-month period. Findings were replicated across both measures. Effects were independent of substance use and initial symptom severity and persisted beyond the initial intervention period. Ameliorating

nonclinical psychotic symptoms trajectories beginning in mid-adolescence via a multifaceted psychosocial intervention is possible. Developmental research on nonclinical psychotic symptoms and their prognostic value should be complemented by more psychosocial intervention research aimed at modifying these symptom trajectories early in their natural history. Clinical trial registration information-Juvenile Justice Girls Randomized Control Trial: Young Adult Follow-up; <http://clinicaltrials.gov; NCT01341626>

Guideline-concordant Management Of Opioid Therapy Among Human Immunodeficiency Virus (HIV)-infected and Uninfected Veterans Gaither JR, Goulet JL, Becker WC, Crystal S, Edelman EJ, Gordon K, Kerns RD, Rimland D, Skanderson M, Weisberg DF, Justice AC, Fiellin DA. *J Pain*. 2014; 15(11): 1130-1140.

Whether patients receive guideline-concordant opioid therapy (OT) is largely unknown and may vary based on provider and patient characteristics. The authors assessed the extent to which human immunodeficiency virus (HIV)-infected and uninfected patients initiating long-term (≥ 90 days) OT received care concordant with American Pain Society/American Academy of Pain Medicine and Department of Veterans Affairs/Department of Defense guidelines by measuring receipt of 17 indicators during the first 6 months of OT. Of 20,753 patients, HIV-infected patients ($n = 6,604$) were more likely than uninfected patients to receive a primary care provider visit within 1 month (52.0% vs 30.9%) and 6 months (90.7% vs 73.7%) and urine drug tests within 1 month (14.8% vs 11.5%) and 6 months (19.5% vs 15.4%; all $P < .001$). HIV-infected patients were also more likely to receive OT concurrent with sedatives (24.6% vs 19.6%) and a current substance use disorder (21.6% vs 17.2%). Among both patient groups, only modest changes in guideline concordance were observed over time: urine drug tests and OT concurrent with current substance use disorders increased, whereas sedative co-prescriptions decreased (all P s for trend $< .001$). Over a 10-year period, on average, patients received no more than 40% of recommended care. OT guideline-concordant care is rare in primary care, varies by patient/provider characteristics, and has undergone few changes over time. The promulgation of OT clinical guidelines has not resulted in substantive changes over time in OT management, which falls well short of the standard recommended by leading medical societies. Strategies are needed to increase the provision of OT guideline-concordant care for all patients.

Current Practices Of Screening For Incident Hepatitis C Virus (HCV) Infection Among HIV-infected, HCV-uninfected Individuals In Primary Care Freiman JM, Huang W, White LF, Geng EH, Hurt CB, Taylor LE, Overton ET, Cachay ER, Kitahata MM, Moore RD, Rodriguez B, Mayer KH, Linas BP. *Clin Infect Dis*. 2014; 59(12): 1686-1693.

Human immunodeficiency virus (HIV)-infected, hepatitis C virus (HCV)-uninfected patients are at risk for incident HCV infection, but little is known about screening practices for incident HCV among HIV-infected individuals in HIV primary care clinics. The authors used data from the Center for AIDS Research Network of Integrated Clinical Systems (CNICS) to investigate historical trends in screening for incident HCV infection among HIV-infected patients who were HCV-uninfected at enrollment in care. They used descriptive measures and Poisson regression to identify factors associated with screening for HCV infection (using HCV antibody or RNA), performed temporal analyses to assess changes in screening over time, and investigated the frequency with which elevated alanine aminotransferase (ALT) levels were followed by diagnostic HCV testing. Among 17 090 patients registered at CNICS sites between 2000 and 2011, 14 534 (85%) received HCV antibody screening within 3 months of enrolling in care, and 9077 met all of the inclusion criteria.

Only 55.6% ever received additional HCV screening. HCV screening increased over time, but not uniformly at all sites. Only 26.7% of first-time ALT elevations to >100 IU/L were followed up within 12 months by HCV antibody or RNA testing. Although most HIV-infected patients were screened for prevalent HCV infection at enrollment in care, only half who were HCV uninfected were screened again. Screening varied between sites, even when controlling for demographics and risk behaviors. Patients with new ALT elevations to >100 IU/L were seldom assessed for incident HCV infection. Guidelines are needed to help HIV providers know whom to screen, how frequently to screen, and which screening test to use.

Cost-effectiveness Of Rapid Hepatitis C Virus (HCV) Testing and Simultaneous Rapid HCV And HIV Testing In Substance Abuse Treatment Programs Schackman BR, Leff JA, Barter DM, DiLorenzo MA, Feaster DJ, Metsch LR, Freedberg KA, Linas BP. *Addiction*. 2015; 110(1): 129-143.

The objective of this study was to evaluate the cost-effectiveness of rapid hepatitis C virus (HCV) and simultaneous HCV/HIV antibody testing in substance abuse treatment programs. The authors used a decision analytic model to compare the cost-effectiveness of no HCV testing referral or offer, off-site HCV testing referral, on-site rapid HCV testing offer and on-site rapid HCV and HIV testing offer. Base case inputs included 11% undetected chronic HCV, 0.4% undetected HIV, 35% HCV co-infection among HIV-infected, 53% linked to HCV care after testing antibody-positive and 67% linked to HIV care. Disease outcomes were estimated from established computer simulation models of HCV [Hepatitis C Cost-Effectiveness (HEP-CE)] and HIV [Cost-Effectiveness of Preventing AIDS Complications (CEPAC)]. Data on test acceptance and costs were from a national randomized trial of HIV testing strategies conducted at 12 substance abuse treatment programs in the United States. Lifetime costs (2011 US\$) and quality-adjusted life years (QALYs) discounted at 3% annually; incremental cost-effectiveness ratios (ICERs). On-site rapid HCV testing had an ICER of \$18,300/QALY compared with no testing, and was more efficient than (dominated) off-site HCV testing referral. On-site rapid HCV and HIV testing had an ICER of \$64,500/QALY compared with on-site rapid HCV testing alone. In one- and two-way sensitivity analyses, the ICER of on-site rapid HCV and HIV testing remained <\$100,000/QALY, except when undetected HIV prevalence was <0.1% or when we assumed frequent HIV testing elsewhere. The ICER remained <\$100,000/QALY in 91% of probabilistic sensitivity analyses. On-site rapid hepatitis C virus and HIV testing in substance abuse treatment programs is cost-effective at a <\$100,000/quality-adjusted life year threshold.

DIVISION OF PHARMACOTHERAPIES AND MEDICAL CONSEQUENCES OF DRUG ABUSE (DPMCDA)

Chronic Cocaine Use and Its Association With Myocardial Steatosis Evaluated By 1H Magnetic Resonance Spectroscopy In African Americans Lai S, Gerstenblith G, Li J, Zhu H, Bluemke DA, Liu CY, Zimmerman SL, Chen S, Lai H, Treisman G. *J Addict Med*. 2015; 9(1): 31-39.

Cardiac steatosis is a manifestation of ectopic fat deposition and is associated with obesity. The impact of chronic cocaine use on obesity measures and on the relationship between obesity measures and cardiac steatosis is not well-characterized. The objectives of this study were to compare obesity measures in chronic cocaine users and nonusers, and to explore which factors, in

addition to obesity measures, are associated with myocardial triglyceride in African Americans, using noninvasive magnetic resonance spectroscopy. Between June 2004 and January 2014, 180 healthy African American adults without HIV infection, hypertension, and diabetes were enrolled in an observational proton magnetic resonance spectroscopy and imaging study investigating factors associated with cardiac steatosis. Among these 180 participants, 80 were chronic cocaine users and 100 were nonusers. The median age was 42 (interquartile range, 34-47) years. Obesity measures trended higher in cocaine users than in nonusers. The median myocardial triglyceride was 0.6% (interquartile range, 0.4%-1.1%). Among the factors investigated, years of cocaine use, leptin, and visceral fat were independently associated with myocardial triglyceride. Body mass index and visceral fat, which were significantly associated with myocardial triglyceride in noncocaine users, were not associated with myocardial triglyceride content in cocaine users. This study shows (1) cocaine users may have more fat than nonusers and (2) myocardial triglyceride is independently associated with duration of cocaine use, leptin, and visceral fat in all subjects, whereas leptin and high-density lipoprotein cholesterol, but not visceral fat or body mass index, in cocaine users, suggesting that chronic cocaine use may modify the relationships between obesity measures and myocardial triglyceride.

Chronic Cannabinoid Receptor 2 Activation Reverses Paclitaxel Neuropathy Without Tolerance Or Cannabinoid Receptor 1-Dependent Withdrawal

Deng L, Guindon J, Cornett BL, Makriyannis A, Mackie K, Hohmann AG. *Biol Psychiatry*. 2015 Mar; 77(5): 475-487. Mixed cannabinoid receptor 1 and 2 (CB1 and CB2) agonists such as $\Delta(9)$ -tetrahydrocannabinol ($\Delta(9)$ -THC) can produce tolerance, physical withdrawal, and unwanted CB1-mediated central nervous system side effects. Whether repeated systemic administration of a CB2-preferring agonist engages CB1 receptors or produces CB1-mediated side effects is unknown. The authors evaluated antiallodynic efficacy, possible tolerance, and cannabimimetic side effects of repeated dosing with a CB2-preferring agonist AM1710 in a model of chemotherapy-induced neuropathy produced by paclitaxel using CB1 knockout (CB1KO), CB2 knockout (CB2KO), and wild-type (WT) mice. Comparisons were made with the prototypic classic cannabinoid $\Delta(9)$ -THC. They also explored the site and possible mechanism of action of AM1710. Paclitaxel-induced mechanical and cold allodynia developed to an equivalent degree in CB1KO, CB2KO, and WT mice. Both AM1710 and $\Delta(9)$ -THC suppressed established paclitaxel-induced allodynia in WT mice. In contrast to $\Delta(9)$ -THC, chronic administration of AM1710 did not engage CB1 activity or produce antinociceptive tolerance, CB1-mediated cannabinoid withdrawal, hypothermia, or motor dysfunction. Antiallodynic efficacy of systemic administration of AM1710 was absent in CB2KO mice and WT mice receiving the CB2 antagonist AM630, administered either systemically or intrathecally. Intrathecal administration of AM1710 also attenuated paclitaxel-induced allodynia in WT mice, but not CB2KO mice, implicating a possible role for spinal CB2 receptors in AM1710 antiallodynic efficacy. Finally, both acute and chronic administration of AM1710 decreased messenger RNA levels of tumor necrosis factor- α and monocyte chemoattractant protein 1 in lumbar spinal cord of paclitaxel-treated WT mice. These results highlight the potential of prolonged use of CB2 agonists for managing chemotherapy-induced allodynia with a favorable therapeutic ratio marked by sustained efficacy and absence of tolerance, physical withdrawal, or CB1-mediated side effects.

Simultaneous Inhibition Of Fatty Acid Amide Hydrolase (FAAH) and Monoacylglycerol Lipase (MAGL) Shares Discriminative Stimulus Effects With Δ 9-THC In Mice

Hruba L, Seillier A, Zaki A, Cravatt BF, Lichtman AH, Giuffrida A, McMahon LR. *J Pharmacol Exp Ther*. 2015 Feb 24. pii: jpet.115.222836. [Epub ahead of print].

Monoacylglycerol lipase (MAGL) and fatty acid amide hydrolase (FAAH) inhibitors exert pre-clinical effects indicative of therapeutic potential (i.e., analgesia). However, the extent to which MAGL and FAAH inhibitors produce unwanted effects remains unclear. Here, FAAH and MAGL inhibition was examined separately and together in a Δ 9-tetrahydrocannabinol (Δ 9-THC; 5.6 mg/kg i.p.) discrimination assay predictive of subjective effects associated with cannabis use, and the relative contribution of N-arachidonoyl ethanolamine (AEA) and 2-arachidonoylglycerol (2-AG) in the prefrontal cortex, hippocampus, and caudate putamen to those effects was examined. Δ 9-THC dose-dependently increased Δ 9-THC appropriate responses (ED50 value = 3.1 mg/kg), whereas the FAAH inhibitors PF-3845 and URB597 or a MAGL inhibitor JZL184 alone did not substitute for the Δ 9-THC discriminative stimulus. The non-selective FAAH/MAGL inhibitors SA-57 and JZL195 fully substituted for Δ 9-THC with ED50 values equal to 2.7 and 21.8 mg/kg, respectively. Full substitution for Δ 9-THC also was produced by a combination of JZL184 and PF-3845, but not by a combination of JZL184 and URB597 (i.e., 52% maximum). The CB1 receptor antagonist rimonabant attenuated the discriminative stimulus effects of Δ 9-THC, SA-57, JZL195, and the combined effects of JZL184 and PF-3845. Full substitution for the Δ 9-THC discriminative stimulus occurred only when both 2-AG and AEA were significantly elevated, and the patterns of increased endocannabinoid content were similar among brain regions. Overall, these results suggest that increasing both endogenous 2-AG and AEA produces qualitatively unique effects (i.e., the subjective effects of cannabis) that are not obtained from increasing either 2-AG or AEA separately

A Peripheral Endocannabinoid Mechanism Contributes To Glucocorticoid-Mediated Metabolic Syndrome

Bowles NP, Karatsoreos IN, Li X, Vemuri VK, Wood JA, Li Z, Tamashiro KL, Schwartz GJ, Makriyannis AM, Kunos G, Hillard CJ, McEwen BS, Hill MN. *Proc Natl Acad Sci U S A*. 2015 Jan; 112(1): 285-290.

Glucocorticoids are known to promote the development of metabolic syndrome through the modulation of both feeding pathways and metabolic processes; however, the precise mechanisms of these effects are not well-understood. Recent evidence shows that glucocorticoids possess the ability to increase endocannabinoid signaling, which is known to regulate appetite, energy balance, and metabolic processes through both central and peripheral pathways. The aim of this study was to determine the role of endocannabinoid signaling in glucocorticoid-mediated obesity and metabolic syndrome. Using a mouse model of excess corticosterone exposure, the authors found that the ability of glucocorticoids to increase adiposity, weight gain, hormonal dysregulation, hepatic steatosis, and dyslipidemia was reduced or reversed in mice lacking the cannabinoid CB1 receptor as well as mice treated with the global CB1 receptor antagonist AM251. Similarly, a neutral, peripherally restricted CB1 receptor antagonist (AM6545) was able to attenuate the metabolic phenotype caused by chronic corticosterone, suggesting a peripheral mechanism for these effects. Biochemical analyses showed that chronic excess glucocorticoid exposure produced a significant increase in hepatic and circulating levels of the endocannabinoid anandamide, whereas no effect was observed in the hypothalamus. To test the role of the liver, specific and exclusive deletion of hepatic CB1 receptor resulted in a rescue of the dyslipidemic effects of glucocorticoid exposure, while not affecting the obesity phenotype or the elevations in insulin and leptin. Together, these data indicate that glucocorticoids recruit peripheral endocannabinoid signaling to promote

metabolic dysregulation, with hepatic endocannabinoid signaling being especially important for changes in lipid metabolism.

Cannabinoid Withdrawal In Mice: Inverse Agonist Vs Neutral Antagonist Tai S, Nikas SP, Shukla VG, Vemuri K, Makriyannis A, Järbe TU. *Psychopharmacology (Berl)*. 2015 Mar; [Epub ahead of print].

Previous reports shows rimonabant's inverse properties may be a limiting factor for treating cannabinoid dependence. To overcome this limitation, neutral antagonists were developed, to address mechanisms by which an inverse agonist and neutral antagonist elicit withdrawal. The objective of this study is to introduce an animal model to study cannabinoid dependence by incorporating traditional methodologies and profiling novel cannabinoid ligands with distinct pharmacological properties/modes of action by evaluating their pharmacological effects on CB1-receptor (CB1R) related physiological/behavioral endpoints. The cannabinergic AM2389 was acutely characterized in the tetrad (locomotor activity, analgesia, inverted screen/catalepsy bar test, and temperature), with some comparisons made to $\Delta(9)$ -tetrahydrocannabinol (THC). Tolerance was measured in mice repeatedly administered AM2389. Antagonist-precipitated withdrawal was characterized in cannabinoid-adapted mice induced by either centrally acting antagonists, rimonabant and AM4113, or an antagonist with limited brain penetration, AM6545. In the tetrad, AM2389 was more potent and longer acting than THC, suggesting a novel approach for inducing dependence. Repeated administration of AM2389 led to tolerance by attenuating hypothermia that was induced by acute AM2389 administration. Antagonist-precipitated withdrawal signs were induced by rimonabant or AM4113, but not by AM6545. Antagonist-precipitated withdrawal was reversed by reinstating AM2389 or THC. These findings suggest cannabinoid-precipitated withdrawal may not be ascribed to the inverse properties of rimonabant, but rather to rapid competition with the agonist at the CB1R. This withdrawal syndrome is likely centrally mediated, since only the centrally acting CB1R antagonists elicited withdrawal, i.e., such responses were absent after the purported peripherally selective CB1R antagonist AM6545.

The Anti-(+)-Methamphetamine Monoclonal Antibody mAb7F9 Attenuates Acute (+)-Methamphetamine Effects On Intracranial Self-Stimulation In Rats Harris AC, LeSage MG, Shelley D, Perry JL, Pentel PR, Owens SM. *PLoS One*. 2015; 10(3):e0118787.

Passive immunization with monoclonal antibodies (mAbs) against (+)-methamphetamine (METH) is being evaluated for the treatment of METH addiction. A human/mouse chimeric form of the murine anti-METH mAb7F9 has entered clinical trials. This study examined the effects of murine mAb7F9 on certain addiction-related behavioral effects of METH in rats as measured using intracranial self-stimulation (ICSS). Initial studies indicated that acute METH (0.1-0.56 mg/kg, s.c.) lowered the minimal (threshold) stimulation intensity that maintained ICSS. METH (0.3 mg/kg, s.c.) also blocked elevations in ICSS thresholds (anhedonia-like behavior) during spontaneous withdrawal from a chronic METH infusion (10 mg/kg/day x 7 days). In studies examining effects of i.v. pretreatment with mAb7F9 (at 30, 100, or 200 mg/kg), 200 mg/kg blocked the ability of an initial injection of METH (0.3 mg/kg, s.c.) to reduce baseline ICSS thresholds, but was less capable of attenuating the effect of subsequent daily injections of METH. mAb7F9 (200 mg/kg) also produced a small but significant reduction in the ability of METH (0.3 mg/kg, s.c.) to reverse METH withdrawal-induced elevations in ICSS thresholds. These studies demonstrate that mAb7F9 can partially attenuate some addiction-related effects of acute METH in an ICSS model, and provide some support for the therapeutic potential of mAb7F9 for the treatment of METH

addiction.

Pharmacokinetic Correlates Of the Effects Of A Heroin Vaccine On Heroin Self-Administration In Rats Raleigh MD, Pentel PR, LeSage MG. PLoS One. 2014; 9(12):e115696.

The purpose of this study was to evaluate the effects of a morphine-conjugate vaccine (M-KLH) on the acquisition, maintenance, and reinstatement of heroin self-administration (HSA) in rats, and on heroin and metabolite distribution during heroin administration that approximated the self-administered dosing rate. Vaccination with M-KLH blocked heroin-primed reinstatement of heroin responding. Vaccination also decreased HSA at low heroin unit doses but produced a compensatory increase in heroin self-administration at high unit doses. Vaccination shifted the heroin dose-response curve to the right, indicating reduced heroin potency, and behavioral economic demand curve analysis further confirmed this effect. In a separate experiment heroin was administered at rates simulating heroin exposure during HSA. Heroin and its active metabolites, 6-acetylmorphine (6-AM) and morphine, were retained in plasma and metabolite concentrations were reduced in brain in vaccinated rats compared to controls. Reductions in 6-AM concentrations in brain after vaccination were consistent with the changes in HSA rates accompanying vaccination. These data provide evidence that 6-AM is the principal mediator of heroin reinforcement, and the principal target of the M-KLH vaccine, in this model. While heroin vaccines may have potential as therapies for heroin addiction, high antibody to drug ratios appear to be important for obtaining maximal efficacy.

Flagellin As Carrier and Adjuvant In Cocaine Vaccine Development Lockner JW, Eubanks LM, Choi JL, Lively JM, Schlosburg JE, Collins KC, Globisch D, Rosenfeld-Gunn RJ, Wilson IA, Janda KD. Mol Pharm. 2015 Feb;12(2): 653-662.

Cocaine abuse is problematic, directly and indirectly impacting the lives of millions, and yet existing therapies are inadequate and usually ineffective. A cocaine vaccine would be a promising alternative therapeutic option, but efficacy is hampered by variable production of anticocaine antibodies. Thus, new tactics and strategies for boosting cocaine vaccine immunogenicity must be explored. Flagellin is a bacterial protein that stimulates the innate immune response via binding to extracellular Toll-like receptor 5 (TLR5) and also via interaction with intracellular NOD-like receptor C4 (NLRC4), leading to production of pro-inflammatory cytokines. Reasoning that flagellin could serve as both carrier and adjuvant, we modified recombinant flagellin protein to display a cocaine hapten termed GNE. The resulting conjugates exhibited dose-dependent stimulation of anti-GNE antibody production. Moreover, when adjuvanted with alum, but not with liposomal MPLA, GNE-FliC was found to be better than our benchmark GNE-KLH. This work represents a new avenue for exploration in the use of hapten-flagellin conjugates to elicit antihapten immune responses.

Bupropion For the Treatment Of Methamphetamine Dependence In Non-Daily Users: A Randomized, Double-Blind, Placebo-Controlled Trial Anderson AL, Li SH, Markova D, Holmes TH, Chiang N, Kahn R, Campbell J, Dickerson DL, Galloway GP, Haning W, Roache JD, Stock C, Elkashef AM. Drug Alcohol Depend. 2015 Feb 7. pii: S0376-8716(15)00056-3. doi: 10.1016/j.drugalcdep.2015.01.036. [Epub ahead of print].

Bupropion was tested for efficacy to achieve methamphetamine (MA) abstinence in dependent, non-daily users. A randomized, double-blind, placebo-controlled trial, with 12-week treatment and 4-week follow-up, was conducted with 204 treatment-seeking participants having MA dependence

per DSM-IV, who used MA on a less-than-daily basis. 104 were randomized to matched placebo and 100 to bupropion, sustained-release 150mg, twice daily. Participants were seen three times weekly to obtain urine for MA and bupropion assays, study assessments, and thrice weekly, 90-min, group psychotherapy. There was no biomarker for placebo adherence. The primary outcome was achievement of abstinence throughout the last two weeks of treatment; 'success' requiring at least two urine samples during each of Weeks 11 and 12, and all samples MA-negative (<300ng/mL). Bupropion and placebo groups did not differ significantly in the percentage achieving abstinence for the last 2 weeks of treatment (chi-square, $p=0.32$). Subgroup analysis of participants with lower baseline MA use (≤ 18 of last 30 days before consent) also revealed no difference in success between groups ($p=0.73$). Medication adherence per protocol (detectable bupropion, $>5\text{ng/mL}$, in $\geq 50\%$ of urine samples from Study Weeks 1-10 and $\geq 66\%$ of urine samples from Weeks 11 to 12) was achieved by 47% of participants taking bupropion. These data indicate that bupropion did not increase abstinence in dependent participants who were using MA less-than-daily. Medication non-adherence was a limitation in this trial. Psychosocial therapy remains the mainstay of treatment for MA dependence. Further research on subgroups who may respond to bupropion may be warranted.

[Naltrexone and Bupropion, Alone Or Combined, Do Not Alter the Reinforcing Effects Of Intranasal Methamphetamine](#) Stoops WW, Pike E, Hays LR, Glaser PE, Rush CR. *Pharmacol Biochem Behav.* 2015 Feb; 129 [Epub ahead of print] 45-50.

Naltrexone and bupropion, when administered alone in clinical trials, modestly reduce amphetamine use. Whether combining these drugs would result in greater reductions in methamphetamine taking relative to either drug alone is undetermined. This study examined the influence of naltrexone, bupropion and a naltrexone-bupropion combination on methamphetamine self-administration in humans. Seven subjects reporting recent illicit stimulant use completed a placebo-controlled, crossover, double-blind study in which the reinforcing, subject-rated and physiological effects of intranasal methamphetamine (0, 10 and 30 mg) were assessed during maintenance on placebo, naltrexone (50 mg), bupropion (300 mg/day), and naltrexone combined with bupropion. Methamphetamine maintained responding and produced prototypic subjective and physiological effects (e.g., increased ratings of good effects, elevated systolic blood pressure). Maintenance doses were well tolerated and generally devoid of effects. No maintenance condition reduced methamphetamine self-administration or systematically altered the subject-rated effects of methamphetamine. These outcomes demonstrate the robust behavioral effects of methamphetamine that could make it resistant to pharmacological manipulation. Although these outcomes indicate that this combination may be ineffective for managing methamphetamine use disorder, future work should evaluate longer maintenance dosing, individuals with different levels of amphetamine use, adding this combination to a behavioral platform and other pharmacotherapy combinations for reducing methamphetamine use.

AIDS RESEARCH PROGRAM (ARP)

[Chronic Administration Of \$\Delta\$ 9-Tetrahydrocannabinol Induces Intestinal Anti-Inflammatory MicroRNA Expression During Acute Simian Immunodeficiency Virus Infection Of Rhesus Macaques](#) Chandra LC, Kumar V, Torben W, Vande Stouwe C, Winsauer P, Amedee A, Molina PE, Mohan M. J Virol. 2015 Jan 15; 89(2): 1168-1181. doi: 10.1128/JVI.01754-14. Epub 2014 Nov 5.

Recreational and medical use of cannabis among human immunodeficiency virus (HIV)-infected individuals has increased in recent years. In simian immunodeficiency virus (SIV)-infected macaques, chronic administration of Δ 9-tetrahydrocannabinol (Δ 9-THC) inhibited viral replication and intestinal inflammation and slowed disease progression. Persistent gastrointestinal disease/inflammation has been proposed to facilitate microbial translocation and systemic immune activation and promote disease progression. Cannabinoids including Δ 9-THC attenuated intestinal inflammation in mouse colitis models and SIV-infected rhesus macaques. To determine if the anti-inflammatory effects of Δ 9-THC involved differential microRNA (miRNA) modulation, the authors profiled miRNA expression at 14, 30, and 60 days postinfection (days p.i.) in the intestine of uninfected macaques receiving Δ 9-THC (n=3) and SIV-infected macaques administered either vehicle (VEH/SIV; n=4) or THC (THC/SIV; n=4). Chronic Δ 9-THC administration to uninfected macaques significantly and positively modulated intestinal miRNA expression by increasing the total number of differentially expressed miRNAs from 14 to 60 days p.i. At 60 days p.i., ~28% of miRNAs showed decreased expression in the VEH/SIV group compared to none showing decrease in the THC/SIV group. Furthermore, compared to the VEH/SIV group, THC selectively upregulated the expression of miR-10a, miR-24, miR-99b, miR-145, miR-149, and miR-187, previously been shown to target proinflammatory molecules. NOX4, a potent reactive oxygen species generator, was confirmed as a direct miR-99b target. A significant increase in NOX4⁺ crypt epithelial cells was detected in VEH/SIV macaques compared to the THC/SIV group. The authors speculate that miR-99b-mediated NOX4 downregulation may protect the intestinal epithelium from oxidative stress-induced damage. These results support a role for differential miRNA induction in THC-mediated suppression of intestinal inflammation. Whether similar miRNA modulation occurs in other tissues requires further investigation. Gastrointestinal (GI) tract disease/inflammation is a hallmark of HIV/SIV infection. Previously, the authors showed that chronic treatment of SIV-infected macaques with Δ 9-tetrahydrocannabinol (Δ 9-THC) increased survival and decreased viral replication and infection-induced gastrointestinal inflammation. Here, they show that chronic THC administration to SIV-infected macaques induced an anti-inflammatory microRNA expression profile in the intestine at 60 days p.i. These included several miRNAs bioinformatically predicted to directly target CXCL12, a chemokine known to regulate lymphocyte and macrophage trafficking into the intestine. Specifically, miR-99b was significantly upregulated in THC-treated SIV-infected macaques and confirmed to directly target NADPH oxidase 4 (NOX4), a reactive oxygen species generator known to damage intestinal epithelial cells. Elevated miR-99b expression was associated with a significantly decreased number of NOX4⁺ epithelial cells in the intestines of THC-treated SIV-infected macaques. Overall, these results show that selective upregulation of anti-inflammatory miRNA expression contributes to THC-mediated suppression of gastrointestinal inflammation and maintenance of intestinal homeostasis.

The Causal Effect Of Opioid Substitution Treatment On HAART Medication Refill

Adherence Nosyk B, Min JE, Colley G, Lima VD, Yip B, Milloy M-JS, Wood E, Montaner JSG
AIDS: Post Acceptance: March 23, 2015; doi:10.1097/QAD.0000000000000642.

People who inject drugs (PWID) account for roughly 13% of the prevalent HIV/AIDS population outside of sub-Saharan Africa, and access to opioid substitution treatment (OST) is limited in many settings globally. OST likely facilitates access to HAART, yet sparse evidence is available to support this hypothesis. The authors' objective was to determine the causal impact of OST exposure on HAART adherence among HIV-positive PWID in a Canadian setting. They executed a retrospective cohort study using linked population-level data for British Columbia, Canada (January 1996-March 2010). We considered HIV-positive PWID after meeting HAART initiation criteria. A marginal structural model was estimated on a monthly timescale using inverse probability of treatment weights. The primary outcome was 95% HAART adherence, according to pharmacy refill compliance. Exposure to OST was defined as 95% of OST receipt, and we controlled for a range of fixed and time-varying covariates. This study included 1852 (63.3%) HIV-positive PWID with a median follow-up of 5.5 years; 34% were female and 39% had previously accessed OST. The baseline covariate-adjusted odds of HAART adherence following OST exposure was 1.96 (95% confidence interval: 1.72-2.24), although the adjusted odds estimated within the marginal structural model was 1.68 (1.48-1.92). Findings were robust to sensitivity analyses on model specification. In a setting characterized by universal healthcare and widespread access to both office-based OST and HAART, OST substantially increased the odds of HAART adherence. This underlines the need to address barriers to OST globally to reduce the disease burden of both opioid dependence and HIV/AIDS.

Compartmentalized Replication Of R5 T Cell-Tropic HIV-1 In the Central Nervous System Early In the Course Of Infection

Sturdevant CB, Joseph SB, Schnell G, Price RW, Swanstrom R, Spudich S. PLoS Pathog. 2015 Mar 26;11(3):e1004720.

Compartmentalized HIV-1 replication within the central nervous system (CNS) likely provides a foundation for neurocognitive impairment and a potentially important tissue reservoir. The timing of emergence and character of this local CNS replication has not been defined in a population of subjects. The authors examined the frequency of elevated cerebrospinal fluid (CSF) HIV-1 RNA concentration, the nature of CSF viral populations compared to the blood, and the presence of a cellular inflammatory response (with the potential to bring infected cells into the CNS) using paired CSF and blood samples obtained over the first two years of infection from 72 ART-naïve subjects. Using single genome amplification (SGA) and phylodynamics analysis of full-length env sequences, the authors compared CSF and blood viral populations in 33 of the 72 subjects. Independent HIV-1 replication in the CNS (compartmentalization) was detected in 20% of sample pairs analyzed by SGA, or 7% of all sample pairs, and was exclusively observed after four months of infection. In subjects with longitudinal sampling, 30% showed evidence of CNS viral replication or pleocytosis/inflammation in at least one time point, and in approximately 16% of subjects we observed evolving CSF/CNS compartmentalized viral replication and/or a marked CSF inflammatory response at multiple time points suggesting an ongoing or recurrent impact of the infection in the CNS. Two subjects had one of two transmitted lineages (or their recombinant) largely sequestered within the CNS shortly after transmission, indicating an additional mechanism for establishing early CNS replication. Transmitted variants were R5 T cell-tropic. Overall, examination of the relationships between CSF viral populations, blood and CSF HIV-1 RNA concentrations, and inflammatory responses suggested four distinct states of viral population

dynamics, with associated mechanisms of local viral replication and the early influx of virus into the CNS. This study considerably enhances the generalizability of the authors' results and greatly expands our knowledge of the early interactions of HIV-1 in the CNS.

Novel Genetic Locus Implicated for HIV-1 Acquisition with Putative Regulatory Links to HIV Replication and Infectivity: A Genome-Wide Association Study

Johnson EO, Hancock DB, Gaddis NC, Levy JL, Page G, Novak SP, Glasheen C, Saccone NL, Rice JP, Moreau MP, Doheny KF, Romm JM, Brooks AI, Aouizerat BE, Bierut LJ, Kral AH. PLoS One. 2015 Mar 18; 10(3):e0118149. doi: 10.1371/journal.pone.0118149. eCollection 2015.

Fifty percent of variability in HIV-1 susceptibility is attributable to host genetics. Thus identifying genetic associations is essential to understanding pathogenesis of HIV-1 and important for targeting drug development. To date, however, CCR5 remains the only gene conclusively associated with HIV acquisition. To identify novel host genetic determinants of HIV-1 acquisition, the authors conducted a genome-wide association study among a high-risk sample of 3,136 injection drug users (IDUs) from the Urban Health Study (UHS). In addition to being IDUs, HIV- controls were frequency-matched to cases on environmental exposures to enhance detection of genetic effects. The authors tested independent replication in the Women's Interagency HIV Study (N=2,533). They also examined publicly available gene expression data to link SNPs associated with HIV acquisition to known mechanisms affecting HIV replication/infectivity. Analysis of the UHS nominated eight genetic regions for replication testing. SNP rs4878712 in FRMPD1 met multiple testing correction for independent replication ($P=1.38 \times 10^{-4}$), although the UHS-WIHS meta-analysis p-value did not reach genome-wide significance ($P=4.47 \times 10^{-7}$ vs. $P < 5.0 \times 10^{-8}$). Gene expression analyses provided promising biological support for the protective G allele at rs4878712 lowering risk of HIV: (1) the G allele was associated with reduced expression of FBXO10 ($r=-0.49$, $P=6.9 \times 10^{-5}$); (2) FBXO10 is a component of the Skp1-Cul1-F-box protein E3 ubiquitin ligase complex that targets Bcl-2 protein for degradation; (3) lower FBXO10 expression was associated with higher BCL2 expression ($r=-0.49$, $P=8 \times 10^{-5}$); (4) higher basal levels of Bcl-2 are known to reduce HIV replication and infectivity in human and animal in vitro studies. These results suggest new potential biological pathways by which host genetics affect susceptibility to HIV upon exposure for follow-up in subsequent studies.

CD4+ T Cell-Dependent Reduction In Hepatitis C Virus-Specific Neutralizing Antibody Responses Following Coinfection With Human Immunodeficiency Virus

Bailey JR, Dowd KA, Snider AE, Osburn WO, Mehta SH, Kirk GD, Thomas DL, Ray SC. J Infect Dis. 2015 Mar 9. pii: jiv139. [Epub ahead of print].

HIV infection leads to lower rates of HCV clearance after acute infection, higher HCV viremia, and accelerated progression of HCV-related fibrosis. The mechanisms underlying this acceleration of HCV progression by HIV are poorly understood, but HIV-induced dysfunction in the anti-HCV humoral immune response may play a role. To define the effect of HIV coinfection on the anti-HCV antibody response, the authors measured anti-HCV envelope (E1E2) binding antibody titers, neutralizing antibody (nAb) titers, and neutralizing antibody breadth of serum from HCV-infected subjects isolated longitudinally before and after incident HIV infection. A significant reduction in HCV envelope-specific binding antibody and neutralizing antibody titers was detected in subjects with $CD4^+$ T cell counts of <350 cells/mm³ after HIV infection, and subjects with $CD4^+$ T cell counts of <200 cells/mm³ also showed a reduction in nAb breadth. Subjects who maintained ≥ 350 $CD4^+$ T cells/mm³ displayed little to no decline in antibody levels. Depletion of $CD4^+$ T cells by

HIV infection results in a global decline in the anti-HCV envelope antibody response, including binding antibody titers, neutralizing antibody titers, and neutralizing antibody breadth.

CENTER FOR CLINICAL TRIALS NETWORK (CCTN)

[Long-term Outcomes from the National Drug Abuse Treatment Clinical Trials Network Prescription Opioid Addiction Treatment Study](#)

Weiss RD, Potter JS, Griffin ML, Provost SE, Fitzmaurice GM, McDermott KA, Srisarajivakul EN, Dodd DR, Dreifuss JA, McHugh RK, Carroll KM. *Drug Alcohol Depend.* 2015 Mar 6. [Epub ahead of print].

Despite the growing prevalence of prescription opioid dependence, longitudinal studies have not examined long-term treatment response. The current study examined outcomes over 42 months in the Prescription Opioid Addiction Treatment Study (POATS). POATS was a multi-site clinical trial lasting up to 9 months, examining different durations of buprenorphine-naloxone plus standard medical management for prescription opioid dependence, with participants randomized to receive or not receive additional opioid drug counseling. A subset of participants (N=375 of 653) enrolled in a follow-up study. Telephone interviews were administered approximately 18, 30, and 42 months after main-trial enrollment. Comparison of baseline characteristics by follow-up participation suggested few differences. At Month 42, much improvement was seen: 31.7% were abstinent from opioids and not on agonist therapy; 29.4% were receiving opioid agonist therapy, but met no symptom criteria for current opioid dependence; 7.5% were using illicit opioids while on agonist therapy; and the remaining 31.4% were using opioids without agonist therapy. Participants reporting a lifetime history of heroin use at baseline were more likely to meet DSM-IV criteria for opioid dependence at Month 42 (OR=4.56, 95% CI=1.29-16.04, $p<.05$). Engagement in agonist therapy was associated with a greater likelihood of illicit-opioid abstinence. Eight percent ($n=27/338$) used heroin for the first time during follow-up; 10.1% reported first-time injection heroin use. The authors conclude that long-term outcomes for those dependent on prescription opioids demonstrated clear improvement from baseline. However, a subset exhibited a worsening course, by initiating heroin use and/or injection opioid use.

[An Electronic Screen for Triaging Adolescent Substance Use by Risk Levels](#)

Levy S, Weiss R, Sherritt L, Ziemnik R, Spalding A, Van Hook S, Shrier LA. *JAMA Pediatr.* 2014 Sep; 168(9): 822-828.

Screening adolescents for substance use and intervening immediately can reduce the burden of addiction and substance-related morbidity. Several screening tools have been developed to identify problem substance use for adolescents, but none have been calibrated to triage adolescents into clinically relevant risk categories to guide interventions. The objective of this study was to describe the psychometric properties of an electronic screen and brief assessment tool that triages adolescents into 4 actionable categories regarding their experience with nontobacco substance use. Adolescent patients (age range, 12-17 years) arriving for routine medical care at 2 outpatient primary care centers and 1 outpatient center for substance use treatment at a pediatric hospital completed an electronic screening tool from June 1, 2012, through March 31, 2013, that consisted of a question on the frequency of using 8 types of drugs in the past year (Screening to Brief Intervention). Additional questions assessed severity of any past-year substance use. Patients completed a structured diagnostic interview (Composite International Diagnostic Interview-

Substance Abuse Module), yielding Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition) substance use diagnoses. For the entire screen and the Screening to Brief Intervention, sensitivity and specificity for identifying nontobacco substance use, substance use disorders, severe substance use disorders, and tobacco dependence were calculated using the Composite International Diagnostic Interview-Substance Abuse Module as the criterion standard. Of 340 patients invited to participate, 216 (63.5%) enrolled in the study. Sensitivity and specificity were 100% and 84% (95% CI, 76%-89%) for identifying nontobacco substance use, 90% (95% CI, 77%-96%) and 94% (95% CI, 89%-96%) for substance use disorders, 100% and 94% (95% CI, 90%-96%) for severe substance use disorders, and 75% (95% CI, 52%-89%) and 98% (95% CI, 95%-100%) for nicotine dependence. No significant differences were found in sensitivity or specificity between the full tool and the Screening to Brief Intervention. A single screening question assessing past-year frequency use for 8 commonly misused categories of substances appears to be a valid method for discriminating among clinically relevant risk categories of adolescent substance use.

[Initial Response as a Predictor of 12-week Buprenorphine-Naloxone Treatment Response in a Prescription Opioid-Dependent Population](#) McDermott KA, Griffin ML, Connery HS, Hilario EY, Fiellin DA, Fitzmaurice GM, Weiss RD. *J Clin Psychiatry*. 2015 Feb; 76(2): 189-194.

Initial medication response has been shown to predict treatment outcome across a variety of substance use disorders, but no studies have examined the predictive power of initial response to buprenorphine-naloxone in the treatment of prescription opioid dependence. The authors therefore conducted a secondary analysis of data from the Prescription Opioid Addiction Treatment Study to determine whether initial response to buprenorphine-naloxone predicted 12-week treatment outcome in a prescription opioid-dependent population. Using data from a multisite, randomized controlled trial of buprenorphine-naloxone plus counseling for DSM-IV prescription opioid dependence (June 2006-July 2009), the authors conducted a secondary analysis to investigate the relationship between initial medication response and 12-week treatment outcome to establish how soon the efficacy of buprenorphine-naloxone could be predicted (N = 360). Outcomes were determined from the Substance Use Report, a self-report measure of substance use, and confirmatory urinalysis. Predictive values were calculated to determine the importance of abstinence versus use at various time points within the first month of treatment (week 1, weeks 1-2, 1-3, or 1-4) in predicting successful versus unsuccessful treatment outcome (based on abstinence or near-abstinence from opioids) in the last 4 weeks of buprenorphine-naloxone treatment (weeks 9-12). Outcome was best predicted by medication response after 2 weeks of treatment. Two weeks of initial abstinence was moderately predictive of treatment success (positive predictive value = 71%), while opioid use in both of the first 2 weeks was strongly predictive of unsuccessful treatment outcome (negative predictive value [NPV] = 84%), especially when successful outcome was defined as total abstinence from opioids in weeks 9-12 (NPV = 94%). The authors conclude that evaluating prescription opioid-dependent patients after 2 weeks of buprenorphine-naloxone treatment may help determine the likelihood of successful outcome at completion of the current treatment regimen. TRIAL REGISTRATION: ClinicalTrials.gov identifier: NCT00316277.

[Using Behavioral Economics to Predict Opioid Use during Prescription Opioid Dependence Treatment](#) Worley MJ, Shoptaw SJ, Bickel WK, Ling W. *Drug Alcohol Depend*. 2015 Mar 1; 148: 62-68. Epub 2014 Dec 30.

Research grounded in behavioral economics has previously linked addictive behavior to disrupted decision-making and reward-processing, but these principles have not been examined in

prescription opioid addiction, which is currently a major public health problem. This study examined whether pre-treatment drug reinforcement value predicted opioid use during outpatient treatment of prescription opioid addiction. Secondary analyses examined participants with prescription opioid dependence who received 12 weeks of buprenorphine-naloxone and counseling in a multi-site clinical trial (N=353). Baseline measures assessed opioid source and indices of drug reinforcement value, including the total amount and proportion of income spent on drugs. Weekly urine drug screens measured opioid use. Obtaining opioids from doctors was associated with lower pre-treatment drug spending, while obtaining opioids from dealers/patients was associated with greater spending. Controlling for demographics, opioid use history, and opioid source frequency, patients who spent a greater total amount (OR=1.30, $p<.001$) and a greater proportion of their income on drugs (OR=1.31, $p<.001$) were more likely to use opioids during treatment. The authors conclude that individual differences in drug reinforcement value, as indicated by pre-treatment allocation of economic resources to drugs, reflects propensity for continued opioid use during treatment among individuals with prescription opioid addiction. Future studies should examine disrupted decision-making and reward-processing in prescription opioid users more directly and test whether reinforcer pathology can be remediated in this population.

[NIDA Clinical Trials Network Common Data Elements Initiative: Advancing Big-Data Addictive-Disorders Research](#) Ghitza UE, Gore-Langton RE, Lindblad R, Tai B.

Front Psychiatry. 2015 Mar 3; 6: 33. eCollection 2015.

The Clinical Trials Network (CTN) of the National Institute on Drug Abuse (NIDA) recently launched a public portal (<http://cde.drugabuse.gov>) (1), which provides a single-source repository for CTN-recommended common data elements (CDEs) for substance use disorders (SUD) for use in electronic health record systems (EHRs) and clinical research. A CDE in this context is a data element consisting of a question and enumerated set of possible values for responses precisely defined by standardized metadata descriptors. CDEs consisting of individual question/answer pairs can be combined into more complex questionnaires and case report forms or used when gathering medical information in the context of providing clinical care. Thus, CDEs describe semantic characteristics for a discrete piece of data, which will be collected, stored, or exchanged during the course of a study or health examination. This will facilitate exchange of standardized data because of the use of CDEs. In this manner, NIDA CDEs can be commonly applied to multiple data collection systems whether in research or clinical care and across different institutions, such that their intentional commonality with use of common data standards can improve data quality, facilitate data re-purposing, and promote data sharing. This paper describes objectives and importance of the CTN CDEs initiative and portal to translational psychiatric research: To support harmonized use of EHR-compatible common data elements to enable exchange and integration of data to answer clinically meaningful questions of broad interest to SUD treatment research, thereby facilitating big-data biomedical science crossing boundaries between research and clinical care.

WOMEN AND GENDER

Increasing Progesterone Levels are Associated with Smoking Abstinence among Free-cycling Women Smokers who Receive Brief Pharmacotherapy Saladin ME, McClure EA, Baker NL, Carpenter MJ, Ramakrishnan V, Hartwell KJ, Gray KM. *Nicotine Tob Res.* 2015 Apr; 17(4):398-406.

Preclinical and human laboratory research suggests that (a) progesterone may decrease drug reward, craving, and smoking behavior, and (b) estradiol may enhance drug reward and smoking behavior. A modest majority of treatment research examining the relationship between menstrual cycle phase and outcomes suggests that the luteal menstrual phase, with its uniquely higher progesterone levels, is associated with better cessation outcomes. However, no studies to date have examined the effects of naturally occurring variation in progesterone and estradiol levels on medication-assisted smoking cessation. The present study sought to fill this notable gap in the treatment literature. Weekly plasma progesterone and estradiol levels were obtained from nicotine-dependent female smokers enrolled in a 4-week cessation trial. Participants (N = 108) were randomized to receive a 4-week course of either varenicline (VAR) tablets and placebo patches or placebo tablets and nicotine patches. Plasma samples were obtained 1 week before their cessation attempt and weekly during medication administration. Abstinence was assessed weekly. Weekly hormone data replicated commonly observed menstrual cycle patterns of progesterone and estradiol levels. Importantly, increases in progesterone level were associated with a 23% increase in the odds for being abstinent within each week of treatment. This effect was driven primarily by nicotine patch-treated versus VAR-treated females. This study was the first to identify an association between progesterone level (increasing) and abstinence outcomes in free-cycling women smokers who participated in a medication-based treatment. Furthermore, the potential benefits of progesterone may vary across different pharmacotherapies. Implications of these findings for smoking cessation intervention are discussed.

An Exploratory Short-term Double-blind Randomized Trial of Varenicline versus Nicotine Patch for Smoking Cessation in Women Gray KM, McClure EA, Baker NL, Hartwell KJ, Carpenter MJ, Saladin ME. *Addiction.* 2015 Mar 1. [Epub ahead of print].

Within a parent study examining ovarian hormone effects on smoking cessation in women, the authors conducted an exploratory short-term trial of varenicline versus transdermal nicotine patch. This was a double-blind double-dummy randomized trial conducted at a single-site outpatient research clinic in the United States. Participants were female smokers, ages 18-45 and averaging ≥ 10 cigarettes per day for at least 6 months (N = 140). Participants were randomized to receive a four-week course of (a) varenicline tablets and placebo patches (n = 67), or (b) placebo tablets and nicotine patches (n = 73). Two brief cessation counseling sessions were provided for all participants. The outcome of primary clinical interest was two-week end-of-treatment abstinence. Secondary outcomes included one- and four-week end-of treatment abstinence and abstinence at a post-treatment follow-up visit occurring four weeks after treatment conclusion. Breath carbon monoxide (≤ 10 parts per million) was used to confirm biochemically self-reported abstinence. Two-week end-of-treatment abstinence was achieved by 37.3% (25/67) of varenicline participants and by 17.8% (13/73) of nicotine patch participants (odds ratio [OR] (95% confidence interval [CI]) 2.7 (1.3-6.0), p = 0.011). One-week (44.8% vs 20.6%, OR 3.1 (1.5-6.6), p = 0.003) and four-week (22.4% vs 9.6%, OR 2.7 (1.0-7.2), p = 0.043) end-of-treatment abstinence similarly favored varenicline, though post-treatment follow-up Russell Standard abstinence was not significantly different

between groups (23.9% vs 13.7%, OR 2.0 (0.8-4.7), $p = 0.126$). In an exploratory four-week head-to-head trial in female smokers, varenicline, compared with nicotine patch, more than doubled the odds of end-of-treatment abstinence, although this diminished somewhat at post-treatment follow-up.

INTRAMURAL RESEARCH PROGRAM (IRP)

[Clonidine Maintenance Prolongs Opioid Abstinence and Decouples Stress From Craving In Daily Life: A Randomized Controlled Trial With Ecological Momentary Assessment](#)

Kowalczyk WJ, Phillips KA, Jobes ML, Kennedy AP, Ghitza UE, Agage DA, Schmittner JP, Epstein DH, Preston KL. *Am J Psychiatry*. 2015 Mar 17:appiajp201414081014. [Epub ahead of print].

The authors tested whether clonidine blocks stress-induced seeking of heroin and cocaine. The study was also intended to confirm translational findings from a rat model of drug relapse by using ecological momentary assessment of patients' stress to test hypotheses about clonidine's behavioral mechanism of action. The authors conducted a randomized double-blind placebo-controlled clinical trial with 208 opioid-dependent patients at an outpatient buprenorphine clinic. The 118 participants (57%) who maintained abstinence during weeks 5–6 were continued on buprenorphine and randomly assigned to receive clonidine (N=61) or placebo (N=57) for 14 weeks. Urine was tested thrice weekly. Lapse was defined as any opioid- positive or missed urine test, and relapse as two or more consecutive lapses. Time to lapse and relapse were examined with Cox regressions; longest period of abstinence was examined with a t test, and ecological momentary assessment data were examined with generalized linear mixed models. In an intent-to-treat analysis, clonidine produced the longest duration (in consecutive days) of abstinence from opioids during the intervention phase (34.8 days [SD=3.7] compared with 25.5 days [SD=2.7]; Cohen's $d=0.38$). There was no group difference in time to relapse, but the clonidine group took longer to lapse (hazard ratio=0.67, 95% CI=0.45–1.00). Ecological momentary assessment showed that daily-life stress was partly decoupled from opioid craving in the clonidine group, supporting the authors' hypothesized mechanism for clonidine's benefits. Clonidine, a readily available medication, is useful in opioid dependence not just for reduction of withdrawal signs, but also as an adjunctive maintenance treatment that increases duration of abstinence. Even in the absence of physical withdrawal, it decouples stress from craving in everyday life.

[Central Role For the Insular Cortex In Mediating Conditioned Responses To Anticipatory Cues](#) Kusumoto-Yoshida I, Liu H, Chen BT, Fontanini A, Bonci A. *Proc Natl Acad Sci U S A*. 2015 Jan 27;112(4): 1190-1195.

Reward-related circuits are fundamental for initiating feeding on the basis of food-predicting cues, whereas gustatory circuits are believed to be involved in the evaluation of food during consumption. However, accumulating evidence challenges such a rigid separation. The insular cortex (IC), an area largely studied in rodents for its role in taste processing, is involved in representing anticipatory cues. Although IC responses to anticipatory cues are well established, the role of IC cue-related activity in mediating feeding behaviors is poorly understood. Here, the authors examined the involvement of the IC in the expression of cue-triggered food approach in mice trained with a Pavlovian conditioning paradigm. They observed a significant change in neuronal firing during presentation of the cue. Pharmacological silencing of the IC inhibited food port approach. Such a

behavior could be recapitulated by temporally selective inactivation during the cue. These findings represent the first evidence, to the authors' knowledge, that cue-evoked neuronal activity in the mouse IC modulates behavioral output, and demonstrate a causal link between cue responses and feeding behaviors.

R-Modafinil Attenuates Nicotine-Taking and Nicotine-Seeking Behavior In Rats Wang X-F, Bi G-H, He Y, Yang H-J, Gao J-T, Okunola-Bakare OM, Slack RD, Gardner EL, Xi Z-X, Newman AH. *Neuropsychopharmacology* 2015, advance online publication, 11 February 2015; doi:10.1038/npp.2015.24

(±)-Modafinil (MOD) is used clinically for the treatment of sleep disorders and has been investigated as a potential medication for the treatment of psychostimulant addiction. However, the therapeutic efficacy of (±)-MOD for addiction is inconclusive. Herein the authors used animal models of self-administration and in vivo microdialysis to study the pharmacological actions of R-modafinil (R-MOD) and S-modafinil (S-MOD) on nicotine-taking and nicotine-seeking behavior, and mechanisms underlying such actions. They found that R-MOD is more potent and effective than S-MOD in attenuating nicotine self-administration in Long–Evans rats. As Long Evans rats did not show a robust reinstatement response to nicotine, we used alcohol-preferring rats (P-rats) that display much higher reinstatement responses to nicotine than Long–Evans rats. The authors found that R-MOD significantly inhibited intravenous nicotine self-administration, nicotine-induced reinstatement, and nicotine-associated cue-induced drug-seeking behavior in P-rats. R-MOD alone neither sustained self-administration in P-rats previously self-administering nicotine nor reinstated extinguished nicotine-seeking behavior. The in vivo brain microdialysis assays demonstrated that R-MOD alone produced a slow-onset moderate increase in extracellular DA. Pretreatment with R-MOD dose-dependently blocked nicotine-induced dopamine (DA) release in the nucleus accumbens (NAc) in both naive and nicotine self-administering rats, suggesting a DA-dependent mechanism underlying mitigation of nicotine's effects. In conclusion, the present findings support further investigation of R-MOD for treatment of nicotine dependence in humans.

Basal Hippocampal Activity and Its Functional Connectivity Predicts Cocaine Relapse

Adinoff, B, Gu, H Merrick, C, McHugh, M, Devous, MD, Jeon-Slaughter, H, Lu, H, Yang, Y, Stein, EA. *Biological Psychiatry*, 2015 Jan 30. pii: S0006-3223(15)00045-1. doi: 10.1016/j.biopsych.2014.12.027. [Epub ahead of print].

Cocaine-induced neuroplastic changes may result in a heightened propensity for relapse. Using regional cerebral blood flow (rCBF) as a marker of basal neuronal activity, this study assessed alterations in rCBF and related resting state functional connectivity (rsFC) to prospectively predict relapse in patients following treatment for cocaine use disorder (CUD). Pseudocontinuous arterial spin labeling functional magnetic resonance imaging and resting blood oxygen level-dependent functional magnetic resonance imaging data were acquired in the same scan session in abstinent participants with CUD before residential treatment discharge and in 20 healthy matched control subjects. Substance use was assessed twice weekly following discharge. Relapsed participants were defined as those who used stimulants within 30 days following treatment discharge (n = 22); early remission participants (n = 18) did not. Voxel-wise, whole-brain analysis revealed enhanced rCBF only in the left posterior hippocampus (pHp) in the relapsed group compared with the early remission and control groups. Using this pHp as a seed, increased rsFC strength with the posterior cingulate cortex (PCC)/precuneus was seen in the relapsed versus early remission subgroups. Together, both increased pHp rCBF and strengthened pHp-PCC rsFC predicted relapse with 75%

accuracy at 30, 60, and 90 days following treatment. In CUD participants at risk of early relapse, increased pHP basal activity and pHP-PCC circuit strength may reflect the propensity for heightened reactivity to cocaine cues and persistent cocaine-related ruminations. Mechanisms to mute hyperactivated brain regions and delink dysregulated neural circuits may prove useful to prevent relapse in patients with CUD.

Dopaminergic and Glutamatergic Microdomains In A Subset Of Rodent Mesoaccumbens

Axons Zhang S, Qi J, Li X, Wang HL, Britt JP, Hoffman AF, Bonci A, Lupica CR, Morales M. Nat Neurosci. 2015 Mar;18(3):386-92. doi: 10.1038/nn.3945. Epub 2015 Feb 9.

Mesoaccumbens fibers are thought to co-release dopamine and glutamate. However, the mechanism is unclear, and co-release by mesoaccumbens fibers has not been documented. Using electron microscopy, the authors found that some mesoaccumbens fibers have vesicular transporters for dopamine (VMAT2) in axon segments that are continuous with axon terminals that lack VMAT2, but contain vesicular glutamate transporters type 2 (VGluT2). In vivo overexpression of VMAT2 did not change the segregation of the two vesicular types, suggesting the existence of highly regulated mechanisms for maintaining this segregation. The mesoaccumbens axon terminals containing VGluT2 vesicles make asymmetric synapses, commonly associated with excitatory signaling. Using optogenetics, the authors found that dopamine and glutamate were released from the same mesoaccumbens fibers. These findings reveal a complex type of signaling by mesoaccumbens fibers in which dopamine and glutamate can be released from the same axons, but are not normally released at the same site or from the same synaptic vesicles.

NIH/HHS POLICY UPDATES

For a complete list see <http://grants.nih.gov/grants/policy/policy.htm>

2015

- April 20 [Request for Information: NIH Precision Medicine Cohort](#)
- April 15 [Reminder: NIH Policy on Application Compliance](#)
- April 10 [Reporting Publications in the Research Performance Progress Report \(RPPR\)](#)
- April 9 [Notice of Potential Delays to NIH Issuing Awards in May 2015](#)
- April 8 [Racial and Ethnic Categories and Definitions for NIH Diversity Programs and for Other Reporting Purposes](#)
- April 2 [Request for Information \(RFI\): Optimizing Funding Policies and Other Strategies to Improve the Impact and Sustainability of Biomedical Research](#)
- March 31 [Publication of the Revised NIH Grants Policy Statement \(Rev. 3/31/2015\)](#)
- March 27 [Notice for Use of Cloud Computing Services for Storage and Analysis of Controlled-Access Data Subject to the NIH Genomic Data Sharing \(GDS\) Policy](#)
- March 24 [Reminder: NIH and AHRQ Biosketch Requirements for Due Dates On or After May 25, 2015](#)
- March 20 [Reminder: NIH Grant Applications and the NIH Genomic Data Sharing Policy](#)
- March 18 [New Form To Capture Additional Indirect Costs in Multi-project Grant Applications](#)
- March 17 [Notice of Update to the Public Health Service Policy on Humane Care and Use of Laboratory Animals](#)
- March 17 [Notice Regarding Requirement of Grantees and Contractors to Submit Invention Disclosures, Related Reports and Documents Via iEdison](#)
- March 12 [Use of Updated Inclusion Enrollment Format Now Required for Successful Submission of RPPR](#)
- March 6 [Eye on NIH Policy: OMB Uniform Guidance - What it Means for NIH & You \(Video & Interactive Q&A - March 12, 2015\)](#)
- February 20 [Reinforcing Service to the Biomedical Research Community](#)
- February 5 [NIH Interim General Grant Conditions Implementing New HHS Grants Regulations \(Uniform Guidance\)](#)
- February 3 [Request for Information: Sustaining the Biomedical Workforce and a Potential Emeritus Award for Senior Researchers](#)
- February 2 [Registration Open for the 2015 NIH Regional Seminar on Program Funding and Grants Administration – Baltimore, MD](#)
- January 30 [ASSIST Now an Option for Submission of R03 and R21 Applications](#)
- January 27 [Expanding Support of Unicode Character Set in Grant Applications Submitted after February 17, 2015](#)
- January 27 [Adjustments to NIH and AHRQ Grant Application Due Dates Between February 13 and February 18, 2015](#)

CONGRESSIONAL AFFAIRS SECTION
(Prepared April 24, 2015)

APPROPRIATIONS

The President's FY 2016 Budget proposes \$31.311 billion at the program level for NIH, 3.3% above the enacted FY 2015 program level. For NIDA, the corresponding figures are \$1.047 billion and 3.1%.

CONGRESSIONAL HEARINGS/BRIEFINGS

January 21, 2015 – NIDA staff attended a briefing sponsored the RAND Corporation: Insights About Marijuana Legalization in the United States.

January 21, 2015 – NIDA staff attended a briefing sponsored by the Friends of National Institute of Child Health and Human Development: Opioid Use: Protecting the Most Vulnerable -- Addressing Drug Exposure in Mothers and Newborns.

March 3, 2015 – NIH testified in support of its FY 2016 budget request. This was the annual hearing in front of the House Appropriations Committee, Subcommittee on Labor, Health and Human Services, and Education. This year, NIDA Director Dr. Nora Volkow was among the NIH Institute Directors invited by Dr. Collins to attend with him. Several drug abuse and addiction-related questions were asked by subcommittee members (as well as the Chairman of the full committee, Congressman Hal Rogers (R-KY)).

March 17, 2015 – NIDA's Dr. Susan Weiss and Dr. Maureen Boyle met via conference call with staff from Senator Brian Schatz' (D-HI) office. They reviewed a range of marijuana research topics.

March 18, 2015 – NIDA Director Dr. Nora Volkow met with and briefed staff from the House Energy and Commerce Committee, Subcommittee on Oversight and Investigations. Topic: Opioid abuse and addiction. This subcommittee is holding a series of hearings on the topic.

March 24, 2015 – NIDA's Dr. Susan Weiss, along with representatives from the FDA, Drug Enforcement Administration and the Department of Justice, met with staff from Senator Kirsten Gillibrand (D-NY). The topic was marijuana use and addiction, and the potential therapeutic uses of marijuana.

March 26, 2015 -- The House Energy and Commerce Committee, Subcommittee on Oversight and Investigations, held its first hearing focused on opioids. Transcript, statements and video available at <http://energycommerce.house.gov/press-release/suboversight-continues-its-review-growing-threat-prescription-drug-and-heroin-abuse>.

April 3, 2015 – At their request, the Clerks of the Senate Appropriations Committee, Subcommittee on Labor, Health and Human Services, and Education, visited NIH to meet with several IC directors. NIDA’s Dr. Nora Volkow was one of the Directors who had the opportunity to brief these staff on important work ongoing at the Institute.

April 6-9, 2015 – Fourth Annual Rx Summit – At the request of Appropriations Committee Chairman Hal Rogers (R-KY), NIDA Director Dr. Nora Volkow and NIH Director Dr. Francis Collins provided plenary remarks at this year’s Summit. Over 1400 attendees gathered this year to focus on the opioid abuse, addiction and overdose crisis in the U.S. Also addressing the Summit this year were ONDCP Director Michael Botticelli, HHS Secretary Sylvia Burwell, CDC Director Dr. Tom Frieden, FDA Acting Commissioner Dr. Stephen Ostroff, and former Congressman Patrick Kennedy. Seven members of congressmen also attended and spoke as part of a congressional action panel.

April 9, 2015 – Co-located with the Rx Summit, the second annual summit of Smart Approaches to Marijuana featured remarks from NIDA Director Dr. Nora Volkow. Dr. Volkow gave a talk focused on the health effects of marijuana use.

April 23, 2015 -- The House Energy and Commerce Committee, Subcommittee on Oversight and Investigations, held its second hearing focused on opioids. Transcript, statements and video available at <http://energycommerce.house.gov/press-release/suboversight-continues-work-combat-prescription-drug-and-opioid-abuse>.

April 29, 2015 – Senators Rob Portman (R-OH) and Sheldon Whitehouse (D-RI) took the lead in creating and sponsoring the fourth congressional addiction forum. This forum focused on prevention and treatment issues in youth. NIDA’s Dr. Redonna Chandler provided summary remarks on what we know from scientific research on these topics.

LEGISLATION OF INTEREST

H.R. 203 – On January 12, 2015, the House passed the Clay Hunt SAV Act, to direct the Secretary of Veterans Affairs to provide for the conduct of annual evaluations of mental health care and suicide prevention programs of Department of Veterans Affairs, to require a pilot program on loan repayment for psychiatrists who agree to serve in the Veterans Health Administration, and for other purposes. The bill was passed by the Senate on February 3, 2015, and signed into law by the President on February 12, 2015.

H.R. 262 – On January 9, 2015, Representative Barbara Lee (D-CA) introduced the States’ Medical Marijuana Property Rights Protection Act, to amend the Controlled Substances Act so as to exempt real property from civil forfeiture due to medical marijuana-related conduct that is authorized by State law. The bill was referred to the Committees on Judiciary and Energy and Commerce.

H.R. 292 -- On January 13, 2015, Representative Michael Burgess (R-TX) introduced the Advancing Research for Neurological Diseases Act of 2015, to amend the Public Health Service Act to provide for systematic data collection and analysis and epidemiological research regarding

Multiple Sclerosis (MS), Parkinson's disease, and other neurological diseases. The bill was referred to the Committee on Energy and Commerce.

H.R. 467 – On January 22, 2015, Representative Eddie Bernice Johnson (D-TX) introduced the STEM Opportunities Act. Among the provisions, the bill would (1) require the Office of Science and Technology Policy (OSTP) to provide federal science agencies with guidance on establishing specified policies to accommodate the needs of researchers who are caregivers; (2) require each federal science agency to annually collect and submit to the National Science Foundation (NSF) institution-level data on a number of items including demographics, primary field, award type, and review rating (as practicable); (3) direct OSTP, in collaboration with NSF, to identify and disseminate to federal science agencies information and best practices useful in educating program officers and members of standing peer review committees at federal science agencies about research on implicit gender, race, or ethnic bias; and methods to minimize the effect of such bias in federal research grant reviews; and (4) require federal science agencies to maintain or develop and implement policies and practices to minimize the effects of implicit bias in federal research grant reviews. The bill was referred to the House Committee on Science, Space, and Technology.

H.R. 525 -- On January 26, 2015, Representative Massie Thomas (R-KY) introduced the Industrial Hemp Farming Act of 2015, to amend the Controlled Substances Act to exclude industrial hemp from the definition of marijuana, and for other purposes. The bill was referred to the Judiciary Committee and Energy and Commerce Committee. See S.134.

H.R. 667 – On February 3, 2015, Representative Earl Blumenaur (D-OR) introduced the Veterans Equal Access act, to authorize the Department of Veterans Affairs health care providers to provide recommendations and opinions to veterans regarding participation in state medical marijuana programs. The bill was referred to the Committee on Energy and Commerce.

H.R. 953 -- On February 12, 2015, Representative James Sensenbrenner (R-WI) introduced the Comprehensive Addiction Recovery Act, to authorize the Attorney General to award grants to address the national epidemics of prescription drug and heroin abuse. The bill was referred to the committees on the Judiciary and Energy and Commerce. See S. 524.

H.R. 1013 – On February 20, 2015, Representative Jared Polis (D-CO) introduced the Regulate Marijuana like Alcohol Act, to decriminalize marijuana at the federal level, to leave to the states the power to regulate marijuana in a similar way to the way they regulate alcohol, and for other purposes. The bill was referred to several committees: Judiciary, Ways and Means, Energy and Commerce, Natural Resources.

H.R. 1014 – On February 20, 2015, Representative Earl Blumenaur introduced the Marijuana Tax Revenue act of 2015, to amend the IRS code of 1986 to provide for the taxation of marijuana. The bill was referred to the Committee on Ways and Means.

H.R. 1462 – On March 19, 2015, Representative Katherine Clark (D-MA) introduced the Protecting Our Infants Act, to combat the rise of prenatal opioid abuse and neonatal abstinence syndrome. The bill was referred to the Committee on Energy and Commerce. See S.799.

H.R. 1538 – On March 23, 2015, Representative Steve Cohen (D-TN) introduced the CARERS Act, to extend the principle of federalism to State drug policy, provide access to medical marijuana, and enable research into the medicinal properties of marijuana. The bill was referred to the committees on Energy and Commerce, Judiciary, Veterans, and Financial Services. See S.683.

H.R. 1635 – On March 25, 2015, Representative Scott Perry (R-PA) introduced the Charlotte’s Web Medical Access Act of 2015, to amend the controlled substances act to exclude cannabidiol-rich plants from the definition of marijuana. The bill was referred to the committees on Energy and Commerce and Judiciary.

H.R. 1774 – On April 14, 2015, Representative Morgan Griffith (R-VA) introduced the Compassionate Access Act, to provide for the rescheduling of marijuana, the medical use of marijuana in accordance with state law, and the exclusion of cannabidiol from the definition of marijuana. The bill was referred to the committees on Energy and Commerce and Judiciary.

H.R. 1855 – On April 16, 2015, Representative Earl Blumenaur (D-OR) introduced the Small Business Tax Equity act, a bill to amend the Internal Revenue Code of 1986 to allow deductions and credits relating to expenditures in connection with marijuana sales conducted in compliance with State law. The bill was referred to the Committee on Ways and Means. See S. 987.

H.R. 1940 – On April 22, 2015, Representative Dana Rohrbacher (R-CA) introduced a bill to amend the Controlled Substances Act to provide for a new rule regarding the application of the Act to marijuana, and for other purposes. The bill was referred to the Committees on Energy and Commerce, Judiciary.

H.R. 1988 -- On April 23, 2015, Representative Marcia Fudge (D-OH) introduced the Breaking Addiction Act of 2015, to provide for the waiver of the Medicaid IMD limitation in order to permit Medicaid coverage for substance use disorder treatment services furnished to certain individuals in a community-based institution for mental diseases. The bill was referred to the committee on Energy and Commerce.

S. 134 – On January 8, 2015, Senator Ron Wyden (D-OR) introduced the Industrial Hemp Farming Act of 2015, to amend the Controlled Substances Act to exclude industrial hemp from the definition of marijuana, and for other purposes. The bill was referred to the Judiciary Committee. See H.R. 525.

S. 318/H.R. 531– On January 29, 2015, and January 26, 2015, Senator Barbara Mikulski (D-MD) and Representative Rosa DeLauro (D-CT) introduced S. 318 and H.R. 531, respectively, the Accelerating Biomedical Research Act. These bills would prioritize funding for the National Institutes of Health to discover treatments and cures, to maintain global leadership in medical innovation, and to restore the purchasing power the NIH had after the historic doubling campaign that ended in fiscal year 2003. The bills were referred to Senate and House Committees on the Budget.

S. 281 – On January 28, 2015, Senator Roy Blunt (R-MO) introduced a bill to require a Federal agency to include language in certain educational advertising materials indicating that such materials are produced and disseminated at taxpayer expense. The bill was referred to the Senate Committee on Homeland Security and Governmental Affairs.

S. 289 – On January 28, 2015, Senator Richard Durbin (D-IL) introduced the American Cures Act. The bill would authorize additional investment for NIH, CDC, Department of Defense Health Programs, and Veterans Medical & Prosthetics Research Program and also create a budget cap adjustment through the remaining years of the Budget Control Act. The bill was referred to the Senate Committee on the Budget.

S. 320 – On January 29, 2015, Senator Elizabeth Warren (D-MA) introduced S. 320, the Medical Innovation Act. The bill would authorize the collection of supplemental payments increase investments in medical research. The bill was referred to the Senate Committee on Health, Education, Labor and Pensions. See H.R. 744.

S. 524 – On February 12, 2015, Senator Sheldon Whitehouse (D-RI) introduced the Comprehensive Addiction Recovery Act, to authorize the Attorney General to award grants to address the twin epidemics of prescription drug and heroin abuse. The bill was referred to the Judiciary Committee. See H.R. 953.

S.683 – On March 10, 2015, Senator Cory Booker (D-NJ) introduced the CARERS Act, to extend the principle of federalism to State drug policy, provide access to medical marijuana, and enable research into the medicinal properties of marijuana. The bill was referred to the Judiciary Committee. See H.R. 1538.

S. 728 - On March 12, 2015, Senator Charles Schumer (D-NY) introduced the Sober Truth on Preventing Underage Drinking Reauthorization Act, or the STOP Act. This bill would direct the Secretary to continue to conduct research and collect data on the short and long-range impact of alcohol use and abuse upon adolescent brain development and other organ systems as well as work in collaboration with the Directors of NIAAA and NIDA, among other federal officials, on the Interagency Coordinating Committee Annual Report on underage drinking and prevention. This legislation would prohibit making, selling, distributing, or possessing powdered alcohol. The bill was referred to the Senate Committee on Health, Education, Labor, and Pensions.

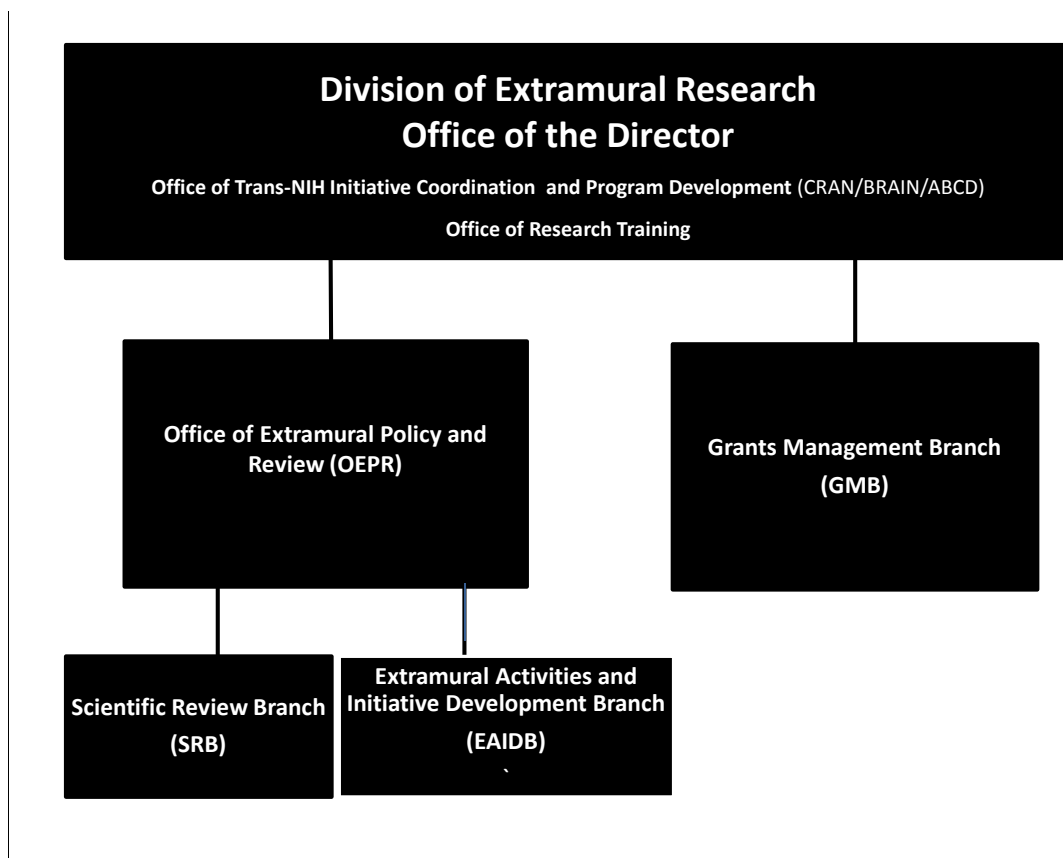
S. 799 – On March 19, 2015, Senator Mitch McConnell (R-KY) introduced the Protecting Our Infants Act, to combat the rise of prenatal opioid abuse and neonatal abstinence syndrome. The bill was referred to the Committee on Health, Education, Labor and Pensions. See H.R. 1462.

S. 987 – On April 16, 2015, Senator Ron Wyden (D-OR) introduced the Small Business Tax Equity Act, to amend the Internal Revenue Code of 1986 to allow deductions and credits relating to expenditures in connection with marijuana sales conducted in compliance with State law. The bill was referred to the Committee on Finance. See H.R. 1855.

DIVISION OF EXTRAMURAL RESEARCH (DER)

In February 2015, NIDA established a new Division with responsibility for overseeing its extramural research and training programs and policies. Functions include:

- Develop, implement, and coordinate NIDA's extramural programs, policies, reviews, and operations planning
- Provide leadership and advice on scientific priorities and strategic goals for NIDA's extramural research programs
- Conduct or coordinate with the Center for Scientific Research (CSR) peer review of all NIDA grant applications
- Oversee [NIDA's research training and early career development program](#)
- Lead NIDA's involvement in vital trans-NIH initiatives, including Collaborative Research on Addiction at NIH (CRAN), the Adolescent Brain Cognitive Development (ABCD) longitudinal study, and Brain Research through Advancing Innovative Neurotechnologies (BRAIN).
- Coordinate and lead activities of the [National Advisory Council on Drug Abuse](#)
- Perform grants management operations, and provide information and guidance for applicants.



PROGRAM ACTIVITIES/FOAS

New NIDA RFAs

On February 10, 2015, NIDA issued an RFA entitled **Advancing Exceptional Research on HIV/AIDS and Substance Abuse (R01) [RFA-DA-16-001](#)**. This FOA will support highly innovative R01 applications on HIV/AIDS and drug abuse and will complement the Avant-Garde Award Program for HIV/AIDS research. The [Avant-Garde award](#) supports individuals who conduct high-risk, high-reward research and does not require a detailed research plan. Applications submitted under this FOA are required to have a detailed research plan and preliminary data. This FOA focuses on innovative research projects that have the potential to open new areas of HIV/AIDS research and/or lead to new avenues for prevention and treatment of HIV/AIDS among substance abusers. The nexus with substance abuse should be clearly described. This FOA is open to both individual researchers and research teams and is not limited to any one area of research on HIV and substance use. Open date: June 30, 2015. Application due date(s): July 31, 2015, by 5:00 PM local time of applicant organization. AIDS application due date(s): July 31, 2015, by 5:00 PM local time of applicant organization.

New NIDA Program Announcements

On April 7, 2015, NIDA issued a PA entitled **Pilot and Feasibility Studies in Preparation for Drug and Alcohol Abuse Prevention Trials (R34) [PA-15-177](#)**. This Funding Opportunity Announcement (FOA) for R34 applications seeks to support: (a) pilot and/or feasibility testing of innovative new, revised, or adapted prevention intervention approaches to prevent or delay the initiation and onset of drug and alcohol use, the progression to problem use or alcohol and other substance use disorder, reduce drinking and driving and deaths related to impaired driving and the drug- or alcohol-related acquisition or transmission of HIV infection and viral hepatitis among diverse populations and settings; and (b) pre-trial feasibility testing for prevention services and systems research. It is expected that research conducted via this R34 mechanism will consist of early stage efficacy, effectiveness or services research that will provide intervention pilot and/or feasibility data that is a pre-requisite for preparing and submitting subsequent applications for larger scale drug or alcohol abuse prevention and/or drug- or alcohol-related HIV prevention intervention studies. This R34 FOA does not support applications for which the sole focus is development of intervention protocols, manuals, or the standardization of protocols; rather, any development work must be imbedded within a pilot/feasibility study. Of particular interest are prevention interventions targeting the healthcare system. Open date: May 16, 2015. Application due date(s): [Standard dates](#) apply, by 5:00 PM local time of applicant organization. AIDS application due date(s): [Standard AIDS dates](#) apply, by 5:00 PM local time of applicant organization.

On March 17, 2015, NIDA issued PAs entitled **International Research Collaboration on Drug Abuse and Addiction Research (R03) [PA-15-141](#), (R01) [PA-15-142](#), (R21) [PA-15-143](#)**. This Funding Opportunity Announcement (FOA) encourages collaborative research applications on drug abuse and addiction that take advantage of special opportunities that exist outside the United States. Special opportunities include access to unusual talent, resources, populations, or environmental

conditions in other countries that will speed scientific discovery. Projects should have relevance to the mission of NIDA and where feasible should address NIDA's international scientific priority areas (<http://www.drugabuse.gov/international/research-priorities>). While the priorities will change from year to year, in FY15 priority areas include: linkages between HIV/AIDS and drug abuse; prevention, initiation, and treatment of nicotine and tobacco use (especially among vulnerable populations such as children, adolescents, pregnant women, and those with co-morbid disorders); the neuroscience of marijuana and cannabinoids; and the effect of changes in laws and policies on marijuana and its impact. Open date: May 5, 2015 (R01), May 16, 2015 (R03, R21). Application due date(s): [Standard dates](#) apply, by 5:00 PM local time of applicant organization. AIDS application due date(s): [Standard AIDS dates](#) apply, by 5:00 PM local time of applicant organization.

On February 13, 2015, NIDA issued a PAR entitled **Identification of Genetic and Genomic Variants by Next-Gen Sequencing in Non-human Animal Models (U01) [PAR-15-120](#)**. The goals of this initiative are to identify gene variants of traits associated with addiction and substance abuse in selectively bred, and outbred non-human animal models using methodologies of Next Gen-Sequencing, mapping, and genotyping. Open date: May 30, 2015. Application due date(s): June 30, 2015; October 20, 2015; March 1, 2016; June 30, 2016; October 20, 2016; March 1, 2017; June 30, 2017; October 20, 2017; March 1, 2018, by 5:00 PM local time of applicant organization. AIDS application due date(s): June 30, 2015; October 20, 2015; March 1, 2016; June 30, 2016; October 20, 2016; March 1, 2017; June 30, 2017; October 20, 2017; March 1, 2018, by 5:00 PM local time of applicant organization.

On February 11, 2015, NIDA issued a PAR entitled **NIDA Mentored Clinical Scientists Development Program Award in Drug Abuse and Addiction (K12) [PAR-15-119](#)**. This funding opportunity announcement (FOA) encourages applications for institutional research career development (K12) programs that propose to support intensive supervised research training and career development experiences for clinician scientists (scholars) leading to research independence in the area of drug abuse and addiction. For this FOA, clinician scientists may include (but are not limited to) physicians, clinical psychologists, epidemiologists, doctoral-level social workers, pharmacists, and behavioral scientists. Scholars are expected to be supported for 3-5 years on consecutive 12-month appointments. Candidates selected for support as scholars must hold a doctorate and commit a minimum of 9 person-months (equivalent to 75% of full-time professional effort) to conducting clinical research and career development activities associated with the proposed program. Open date: May 12, 2015. Application due date(s): June 12, 2015; June 12, 2016; June 12, 2017, by 5:00 PM local time of applicant organization. AIDS application due date(s): September 7, 2015; September 7, 2016; September 7, 2017, by 5:00 PM local time of applicant organization.

On February 5, 2015, NIDA issued PAs entitled **Gene-Environment Interplay in Substance Use Disorders (R01) [PA-15-110](#), (R03) [PA-15-111](#), (R21) [PA-15-112](#)**. This Funding Opportunity Announcement (FOA) seeks to stimulate and expand research on the interplay of genetic and environmental factors in the genesis, course, and outcomes of substance and alcohol use disorders (SUDs). Previous work in genetic epidemiology and molecular genetics has established that SUDs are highly heritable, developmental disorders with important genetic substrates. Building on these findings, new studies using genetically informative approaches are needed to elucidate the complex

interplay of genetic and environmental factors in developmental trajectories of SUDs and comorbid conditions, deepen and refine phenotypic definitions of SUDs, and meet the methodologic challenges of the field. Such studies hold great potential to promote understanding of the true contributions of both genetic and environmental factors to initiation, progression, comorbidity, adverse outcomes, and cessation of SUDs; to elucidate mechanisms of risk; and to enhance opportunities for translation to treatment, prevention, gene-finding and molecular studies. Open date: May 5, 2015 (R01), May 16 (R03, R21). Application due date(s): [Standard dates](#) apply, by 5:00 PM local time of applicant organization. AIDS application due date(s): [Standard AIDS dates](#) apply, by 5:00 PM local time of applicant organization.

New FOAs Issued by the NIH Roadmap

On April 16, 2015, the NIH Common Fund issued a Roadmap RFA entitled **Undiagnosed Diseases Gene Function Research (R21) [RFA-RM-15-004](#)**. This Funding Opportunity intends to support gene function studies in collaboration with the Undiagnosed Diseases Network (UDN) building upon the NIH Intramural Research Program's Undiagnosed Diseases Program (NIH-UDP). Responsive applications will propose to investigate the underlying genetics, biochemistry and/or pathophysiology of newly diagnosed diseases in association with the respective gene variant(s) identified through the UDN. In recent years, gene function studies combined with genetic and genomic analyses and metabolic studies have greatly improved diagnoses of these very rare diseases and advanced scientific knowledge of the underlying pathogenesis. This initiative is funded through the NIH Common Fund, which supports cross-cutting programs that are expected to have exceptionally high impact. Open date: May 24, 2015. Application due date(s): June 24, 2015, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not Applicable.

New FOAs Issued by the NIH Blueprint for Neuroscience Research

Lifespan Human Connectome Project: Baby Connectome (U01) [RFA-MH-16-160](#)

Lifespan Human Connectome Project: Development (U01) [RFA-MH-16-150](#)

Lifespan Human Connectome Project: Aging (U01) [RFA-AG-16-004](#)

New FOAs Issued by the BRAIN INITIATIVE

BRAIN Initiative: Optimization of Novel Tools and Technologies for Neuroscience Research (R44) [PAR-15-121](#)

New RFAs Issued by Other NIH/HHS Components in which NIDA is a participant

NIH-PEPFAR Collaboration on Implementation Science for HIV: Towards an AIDS-free Generation (R01) [RFA-AI-15-020](#)

NIH-PEPFAR Collaboration on Implementation Science for HIV: Towards an AIDS-free Generation (R21) [RFA-AI-15-021](#)

Limited Competition: International epidemiology Databases to Evaluate AIDS (IeDEA) (U01) [RFA-AI-15-017](#)

Big Data to Knowledge (BD2K) Advancing Biomedical Science Using Crowdsourcing and Interactive Digital Media (UH2) [RFA-CA-15-006](#)

New PAs Issued by Other NIH/HHS Components in which NIDA is a participant

Summer Research Education Experience Programs (R25) [PAR-15-184](#)

Jointly Sponsored Ruth L. Kirschstein National Research Service Award Institutional Predoctoral Training Program in the Neurosciences (T32) [PAR-15-178](#)

Administrative Supplements for Research on HIV/AIDS and Aging (Admin Supp) [PA-15-137](#)

Advancing Mechanistic Probiotic/Prebiotic and Human Microbiome Research (R01) [PA-15-135](#)

Advancing Translational and Clinical Probiotic/Prebiotic and Human Microbiome Research (R01) [PA-15-127](#)

Administrative Supplements for Common Basic Sociobehavioral Mechanisms and Processes that Facilitate or Impede Self-Management of Chronic Conditions (Admin Supp) [PA-15-122](#)

New NIH FOAs Issued in Collaboration with the FDA Center for Tobacco Products

On April 23, 2015, NIDA, in collaboration with numerous other NIH components and with the FDA Center for Tobacco Products, issued an RFA entitled **Tobacco Regulatory Science Small Grant Program for New Investigators (R03) [RFA-OD-15-004](#)**. The purpose of this Funding Opportunity Announcement (FOA) is to support [New Investigators](#) in the biomedical, behavioral, and social sciences who are in the early stages of establishing independent careers in tobacco regulatory research. The R03 grant mechanism supports different types of projects including pilot and feasibility studies; secondary analysis of existing data; small, self-contained research projects; development of research methodology; and development of new research technology. Applicants are encouraged to conduct projects that ultimately have potential to inform regulations on tobacco product manufacturing, distribution, and marketing. Research projects must address the research priorities related to the regulatory authority of the Food and Drug Administration (FDA) Center for Tobacco Products (CTP) as mandated by the Family Smoking Prevention and Tobacco Control Act (FSPTCA), Public Law 111-31. Open date: July 20, 2015. Application due date(s): August 20, 2015, February 23, 2016, July 20, 2016, February 23, 2017, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not Applicable.

On April 9, 2015, NIDA, in collaboration with numerous other NIH components and with the FDA Center for Tobacco Products, issued an Administrative Supplement entitled **Administrative Supplements for Tobacco Regulatory Research on Tobacco Flavors and Flavorings (Admin Supp) PA-15-183**. The purpose of this funding opportunity is to generate data regarding the following two topics related to flavors and flavorings in cigarettes, cigars (including little cigars and cigarillos), and e-cigarettes. Only applications proposing research projects relevant to one or more of the two topics will be considered for funding: 1) When tobacco product flavorings and additives are heated or burned, what chemicals are formed from the thermal degradation processes (pyrolysis and/or oxidation), including chemicals that are on the FDA's established [Harmful and Potentially Harmful Constituent list](#), as well as any other toxic chemicals not on the list? What are the levels of the chemicals that are formed? 2) What in vitro assays are capable of comparative toxicological assessments that can examine the harm potential between different flavorings commonly used in cigarettes, cigars and e-cigarettes; comparing the flavorings after burning or heating (at temperatures achieved by conventional pyrolysis and non-conventional heating methods, such as ones used in aerosol formation)? Open date: April 29, 2015. Application due date(s): May 29, 2015 by 5:00 PM local time of applicant organization. AIDS application due date(s): Not Applicable.

Other Program Activities

CTN Update

Seventeen applications in response to the RFA DA-15-008, entitled "The National Drug Abuse Treatment Clinical Trials Network (UG1)," were reviewed on March 31, 2015.

A total of 60 protocols have been initiated since 2001, including multi-site clinical trials (43), multi-site surveys (3), studies in special populations (8), and secondary analyses of data across various trials (6). In addition, 28 ancillary studies have been supported by CTN and non-CTN funds. Over 19,000 participants have been enrolled in CTN studies.

Information on protocols can be found at:

<http://www.drugabuse.gov/about-nida/organization/cctn/ctn/research-studies>

NIDA's Blending Initiative

Accelerating the dissemination of research-based drug abuse treatment into clinical practice is a priority for the National Institute on Drug Abuse (NIDA) and represents the core mission of the Blending Initiative (<http://www.drugabuse.gov/blending-initiative>).

The latest educational effort – *Talking to Patients about Health Risk Behaviors*, continues to reach multiple healthcare providers including physicians, nurses, physician assistants, pharmacists and others. As of February 1, 2015, 41,316 persons have accessed the program and 20,861 certificates have been issued since its October launch. The two programs comprising this novel educational opportunity provide a unique forum where the CME course and the Patient Simulation jointly provide practical guidance for physicians and other clinicians in effective Motivational Interviewing techniques that will facilitate conversations with patients to address Health Risk Behaviors. The CME Course guides physicians and other clinicians through practical skills building and technique

development using videos to model effective communication, while the Patient Simulation allows for real time testing and reinforcement of these skills in the clinical setting. Links to the education are found at <http://www.drugabuse.gov/blending-initiative/cme-ce-simulation>.

Through the Blending Initiative, NIDA partners with professional organizations and other institutions dedicated to the training and education of junior fellows/residents to support the development of expertise in substance use disorders (SUDs) within medical and clinical settings. These training awards aim: 1) to promote knowledge of evidence-based SUD treatment within medical specialties, 2) to advance medical care for patients with substance use disorders, and 3) to facilitate the academic growth, advanced education, and development of future researchers and clinicians in SUDs and medicine and thereby invest in the future of the field. As of the end of 2014, the Blending Initiative has partnered with four organizations to fulfill these goals. These organizations are:

- Society of Teachers of Family Medicine
 - American Academy of Child and Adolescent Psychiatry
 - Society for Adolescent Health and Medicine
 - American College of Emergency Physicians/Emergency Medicine Foundation
- During this period the Blending Initiative supported seminars and exhibits at the following national meetings:

Society for Adolescent Health and Medicine, March 18-21, 2015

American Association for the Treatment of Opioid Dependence, March 28-April 1, 2015

COLLABORATIVE RESEARCH ON ADDICTION (CRAN) ACTIVITIES

Collaborative Research on Addiction at NIH (CRAN) is a consortium of Institutes supporting research on drug use, abuse and addiction. Included are the: National Institute on Alcohol Abuse and Alcoholism (NIAAA), National Institute on Drug Abuse (NIDA), and National Cancer Institute (NCI). For more information about CRAN, see: www.addictionresearch.nih.gov

- A CRAN grantee workshop is planned for Tuesday, and Wednesday, May 12 – 13, 2015, for recipients of administrative or competitive supplements. The workshop will take place at the National Cancer Institute (NCI) Shady Grove Campus in Rockville, Maryland. This meeting is an opportunity for Federal staff and grantees to receive updates on the status of CRAN research as well as some of the difficulties involved in conducting multi-substance research. In addition to poster sessions and oral presentations, we anticipate having several panel discussions involving grantees, CRAN project officers and members of the CRAN coordinating committee.
- A webinar is planned for June 10th, 1PM to 3PM for grantees who were funded under the CRAN RFAs: Using Social Media to Understand and Address Substance Use and Addiction. It will give grantees a chance to learn about each other's projects and progress so far, and to discuss potential areas of shared interest.

Adolescent Brain Cognitive Development (ABCD) Study: FOAs released on February 4th 2015; Application Due Date: April 14, 2015.

- This is a multi-Institute project led by CRAN, in partnership with the Eunice Kennedy Shriver Institute of Child Health and Human Development (NICHD), National Institute of Mental Health (NIMH), National Institute on Minority Health and Health Disparities (NIMHD), Office of Behavioral and Social Sciences Research (OBSSR), National Institute on Neurological Disorders and Stroke (NINDS), and the Office of Research on Women's Health (ORWH).
- The goal of the project is to establish a national, multisite, longitudinal cohort study to prospectively examine the neurodevelopmental and behavioral effects of substance use from early adolescence (approximately age 9-10) through the period of risk for substance use and substance use disorders.
- A collaborative research mechanism is being used for this project (U01, and U54s) and its structure shall consist of three highly integrated components: (1) a set of Research Project Sites; (2) a central Data Analysis and Informatics Center, and (3) a Coordinating Center.
- Technical assistance was provided through a webinar, held on Feb 24, 2015, and available as an audio recording following the webinar, and by the issuance of FAQs.

Drs. Will Aklin, Geetha Subramaniam (NIDA), Brett Hagman (NIAAA) and Annette Kaufman (NCI), as part of a CRAN working group, published a notice to change the age range to include

young adults up to 25 years of age in PA-15-036 "Research Aimed at Novel Behavioral Targets to Improve Adolescent Substance Abuse Treatment and Prevention Interventions (R01) (R34)." Specifically, the original FOA specified inclusion of adolescents. The current revision extends the inclusionary age range to 25 years old based on emerging data on brain development that suggests the brain may not reach full maturity until early or mid-20s (years of age), and because substance use disorders may not emerge until young adulthood. This revision will allow for individual variation in brain development up through a time period when predictable brain development has stabilized.

<http://grants.nih.gov/grants/guide/notice-files/NOT-DA-15-062.html>

<http://grants.nih.gov/grants/guide/notice-files/NOT-DA-15-061.html>

COMMUNICATIONS

PUBLICATIONS & ONLINE RESOURCES

Commonly Abused Drugs Chart: <http://www.drugabuse.gov/drugs-abuse/commonly-abused-drugs> – Revised February 2015

Hallucinogens and Dissociative Drugs Research Report – Revised February 2015

Drugs: Shatter the Myths – Revised March 2015

Step-by-Step Guide for seeking drug abuse treatment (Spanish-language version): <http://www.drugabuse.gov/related-topics/treatment> – March 2015

Easy-to-Read Drug Facts Spanish-language revisions: Marijuana, Cocaine, Heroin, Painkillers, Meth, Alcohol, Cigarettes and tobacco, Other drugs of abuse; <http://easyread.drugabuse.gov/en-espanol.php> – Revised March 2015

Marijuana Research Report – Revised April 2015

Is Marijuana Medicine? (Drug Facts) – Revised April 2015

NIDA NOTES (now online only)

Video: Thomas Kosten talks about the antidrug vaccines, focusing on their potential uses in treatment and prevention, and who may be appropriate candidates for receiving them

NIDA Notes CEU Module: *NIDA Notes* has collaborated with the Institute for Research, Education, and Training in Addictions, to offer social workers and substance abuse clinicians CEU for reading *NIDA Notes* articles. The first educational module focuses on prescription opioids.

Additional selected articles on the NIDA Notes home page report that marijuana may affect future offspring's susceptibility to heroin; some patients who are addicted to opioid painkillers achieve stable abstinence with detoxification followed by naltrexone therapy; methadone and buprenorphine are equally effective for patients addicted to opioid painkillers; parenting education by paraprofessionals yields sustained benefits for children of American Indian teen mothers, may be a model for improving health in resource-poor areas

NIDAMED

This March's issue of *Academic Medicine* features the evaluation of our NIDAMED Centers of Excellence (CoE) for Physician Information interactive module, [The Clinical Assessment of Substance Use Disorders](#) which was created and evaluated by the University of Pennsylvania and

Drexel School of Medicine's CoE. Paul N. Lanken, MD, Dennis H. Novack, MD, Christof Daetwyler, MD, Robert Gallop, PhD, J. Richard Landis, PhD, Jennifer Lapin, PhD, Geetha A. Subramaniam, MD, and Barbara A. Schindler, MD. (March, 2015). Efficacy of an Internet-Based Learning Module and Small-Group Debriefing on Trainees' Attitudes and Communication Skills Toward Patients With Substance Use Disorders: Results of a Cluster Randomized Controlled Trial, *Academic Medicine, Volume 90*, pp: 261-394.

In June, the newly formed NIMDAED Coalition of Healthcare Organizations, including The American Academy of Pediatrics, the California Academy of Family Physicians, the American Society of Addiction Medicine, the American Osteopathic Association, the American Academy of Physician Assistants, and the American Association of Nurse Practitioners, will be meeting with NIDA to develop an adolescent substance use prevention/early intervention continuing medical education/continuing education (CME/CE) module, expected launch Spring 2016.

VIDEOS

- Pain Awareness Month: Dr. Martha Somerman on Research and Pain Management http://youtu.be/TCwLE1_K0qU
- 2015 Reto Nacional sobre el Coeficiente Intelectual (IQ) sobre las Drogas: Respuestas científicas: <http://youtu.be/pzRu6YLBkbl>
- 2015 IQ Challenge: Scientist Answers: <http://youtu.be/jznIvcwkGU4>
- The Herren Project and NIDA team up for National Drug Facts Week: <http://youtu.be/7LQzLLhB6dU>
- Animated Infographic: Monitoring the Future 2014 Survey Results: <https://youtu.be/iQDhYIYp81c>
- NIDA's 2015 Avant-Garde Awards Announced: <https://youtu.be/qVHBOKdLChQ>
- Wilson Compton Discusses Marijuana/SAMSHA Joint Project
- What's New at NIDA: Office of Science Policy and Communication Director's notes for March: <https://youtu.be/aESAqTzTMF0>

CTN-Related Publications

Four editions of the **CTN Bulletin Board** were distributed. The Bulletin Board is an electronic report on the progress of the protocols, committees, and Node activity in the CTN. The Bulletin has wide readership within and outside the CTN and NIDA.

Data from 34 CTN studies and 5 DPMC studies are now available on the **NIDA Data Share website** <http://datashare.nida.nih.gov/>. Over 3,500 data sets have been downloaded by researchers from 72 countries. These data sets are in compliance with HIPAA and CDISC (Clinical Data Interchange Standards Consortium) standards in support of the interoperability required by the NIH Roadmap. The NIDA Data Share is also part of the Neuroscience Information Framework (NIF), which is a dynamic inventory of Web-based neuroscience resources: data, materials, and tools accessible via any computer connected to the Internet.

The **NIDA Common Data Elements (CDE) web portal** (<http://cde.drugabuse.gov/>) provides a single source for CTN recommended CDEs for Substance Use Disorders. All the CDEs displayed on this website are created and housed in the National Cancer Institute (NCI) cancer Data Standards Repository (caDSR) (<https://cdebrowser.nci.nih.gov/CDEBrowser/>). Currently, 17 instruments have been added to this web site with plans to add more.

COMMUNITY AND PRESS EVENTS

2015 Chat Day and National Drug Facts Week (NDFW)

NIDA conducted its annual Chat Day (January 30) and NDFW (January 26-February 1), which included approximately 1500 events in all 50 states and several countries. Over 130 high schools registered for Chat Day and hundreds of questions were answered by NIDA scientists. NIDA developed and distributed press and promotional materials, cultivated radio and organizational partnerships, pitched to select media, coordinated two Radio Media Tours for English and Spanish speaking audiences, and promoted the week via traditional and social media outreach. Visit <http://teens.drugabuse.gov/national-drug-facts-week> for more information.

Population Assessment of Tobacco and Health (PATH) Study

On Thursday, February 26, interim preliminary data on tobacco use from the Population Assessment of Tobacco and Health (PATH) study was presented by NIDA, FDA and Westat staff, as well as the principal investigator. The data was presented during a symposium at the Society for Research on Nicotine & Tobacco 21st Annual Meeting in Philadelphia. NIDA worked in advance of the meeting with FDA staff to prepare talking points and a fact sheet for potential media inquiries. National coverage included stories in *Associated Press* and *Reuters*.

PRESS RELEASES

February 9, 2015 [2015 Avant-Garde Awards offer extraordinary ideas in HIV/AIDS research](#)
March 2, 2015 [Dr. Susan Weiss appointed division director at NIDA](#)

SCIENCE SPOTLIGHTS AND ANNOUNCEMENTS

February 9, 2015 [NIDA researchers discover further complexity in brain reward circuitry](#)
February 11, 2015 [NIDA Director Dr. Nora Volkow to Participate in Facebook Chat about TEDMED Presentation](#)
March 18, 2015 [Medication finds new use in sustaining opioid quit success](#)
March 30, 2015 [Study looks at effects of socioeconomic factors on child brain development and achievement](#)
March 31, 2015 [Research shows that teens and adults are uncertain about legalities of marijuana law in Washington State](#)
April 15, 2015 [Gene variant related to greater difficulty in quitting smoking and earlier lung cancer diagnosis](#)
April 30, 2015 [Medication plus ongoing care provided in emergency departments is promising approach for opioid dependence](#)

MEETINGS/CONFERENCES

Select Meetings and Conferences in which NIDA played a significant role

On April 23, 2015, NIDA again participated in **Take Your Child to Work Day** by having numerous activities both in the Neuroscience Center and on the main NIH campus. Activities included: *Brains Up Close, Animal Brain Matching, Looking through the Microscope, Hands on Science, Brain Science Coloring Contest, Sharpen Your Brain, Dr. Sciencehead and Brain Derby*. In addition, NIDA once again partnered with NIMH staff who sponsored the activity, *Put on Your Thinking Cap*. We also partnered with Archie Fobbs from the National Museum of Health and Medicine who gave an interactive presentation titled *Your Brain – How It Works and What Happens When It's Injured* and with Dr. Mark Burke from Howard University who sponsored *Make a Brain*. Enthusiastic children were able to rotate through the stations and learn about the brain as well as how drugs can impact the brain and body. NIDA and NIMH staff who developed and led the activities included Cathrine Sasek, Stephanie Older, Mary Kautz, Dave Thomas, Roger Sorensen, Heather Kimmel, Maureen Boyle, Kris Bough, Quandra Scudder, Hirsch Davis, Kim DiFonzo, Jen Sizemore, Juli Rose, Josie Anderson, Brian Marquis, Shirley Simson, and Phyllis Quartey-Ampofo.

On March 19, 2015, NIDA participated in the **16th annual Brain Awareness Week** activities at the National Museum of Health and Medicine. Brain Awareness Week is a worldwide celebration of the brain designed to bring neuroscience to children and adults of all ages. NIDA played "*NIDA Brain Derby*," an interactive fast-moving game designed to teach children about drugs of abuse and neuroscience. The grade levels of the children who participated ranged from 5-8th grade. NIDA's game was enthusiastically received and the children not only learned new things, but they also had a great time. The NIDA staff who participated included Drs. Cathrine Sasek, Roger Sorensen, Dave Thomas, Dave White, Rik Kline, Heather Kimmel, and Tessa Hall.

NIDA's Office of Diversity and Health Disparities (ODHD) convened a two-day **NIDA Diversity Supplements Workshop** on Thursday and Friday, April 16-17, 2015, at NIDA Headquarters. The workshop brought together 21 current NIDA diversity supplement recipients at the pre-doctoral, postdoctoral, and early career investigator levels, and 20 undergraduate and post baccalaureate-level students from NIDA's *Diversity-promoting Institutions Drug Abuse Research Program (DIDARP)*, to meet and network with NIDA program staff and senior officials, and with NIDA-funded investigators (among them, former NIDA diversity supplement recipients and program directors of three of NIDA's T32 Programs). Workshop participants received valuable information and guidance on NIDA research priorities and funding opportunities, on graduate school and postdoctoral training opportunities at NIDA's research training sites, and on transitioning to independent research careers. This venue also provided recruitment opportunities for the students who are looking to pursue graduate training in substance abuse research. Poster presentations by current diversity supplement recipients highlighted Day Two of the workshop. Pamela Goodlow of ODHD hosted and coordinated the two-day workshop. Dr. Albert Avila, Director, ODHD, presented overviews of NIDA and ODHD activities, and NIDA and NIH funding opportunities.

The NIDA Office of Diversity and Health Disparities led the **19th Annual 2015 NIDA Summer Research Internship Program**. Coordinated by Julie Huffman, the program was a major success, providing 64 high school and undergraduate students with an eight week summer research experience in NIDA funded research labs across the United States. This year, NIDA received over 360 applications from highly qualified high school and undergraduate students in the area of biomedical, behavioral, clinical and the social sciences as it relates to substance-abuse research. A total of 74 applicants received offers, and 64 students accepted an internship. Selected interns were from all backgrounds including: African-American, American Indian/Alaska Native, Asian-American, Hispanic/Latino, Native Hawaiian/Pacific Islander, and White/Caucasian. The NIDA Summer Internship program is designed to build the research pipeline among our budding scientists. Since its inception, over 815 students have been provided invaluable research opportunities. NIDA funded investigators who volunteered to serve as mentors, as well as NIDA staff who assisted with reviewing applications, were instrumental to the program's success. On February 26-27, 2015, the Office of Diversity and Health Disparities (ODHD) hosted a two-day **Grant Writing and Research Development Workshop** at NIDA in Rockville, Maryland. The overarching goal of the workshop is to provide information on the NIH application and review process aimed at improving the funding of outstanding underrepresented early stage investigators in substance abuse research. Chaired by Dr. Albert Avila, this workshop convened 16 early stage substance abuse investigators, NIDA Program Officials, and NIDA-supported faculty mentors in an intensive workshop setting. During the workshop, new investigators learned of NIDA's research and funding priorities and opportunities, the NIH grants submission and review process, and heard from established investigators on pathways to independence. In addition, participants met individually with NIDA program staff and NIDA funded researchers to receive feedback on their research aims and proposals.

NIDA's Child and Adolescent Workgroup and the Nicotine/Tobacco Interest Group hosted a viewing of the public webinar discussion of the report release of **"Public Health Implications of Raising the Minimum Age of Legal Access to Tobacco Products"** on March 12, 2015 by members of the Institute of Medicine committee at NIDA HQ in Rockville, MD.

The **NIDA CTN Steering Committee Meeting** was held April 14-16, 2015 in Gaithersburg, MD.

Drs. Nancy Pilotte and Roger Sorensen organized a symposium entitled, **"Refining the Circuitry of Addiction with Cutting-Edge Tools"** at the Neuroscience Center in Rockville, MD on April 10, 2015. Presentations include: Investigating the contributions of distinct prefrontal cortex projection subpopulations to drug seeking using optogenetics and rabies tracing (Rachel Smith/Texas A&M University); Circuit and Genetic Tools to Examine Striatal Cell Subtype Mechanisms in Drug Abuse (Mary Kay Lobo/University of Maryland School of Medicine); Balancing Act: Using DREADDs to delineate the neural circuits that regulate addiction and decision-making (Susan Ferguson/Seattle Children's Research Institute); and Cracking addiction circuitry through optogenetic manipulation and cellular-resolution imaging (Ilana Witten/Princeton University)

On March 25 and 26, 2015, NIDA DPMCDAs leadership (David McCann, Phil Skolnick, and Ivan Montoya) presented and chaired sessions during a meeting entitled **"Measures of Outcome for Stimulant Trials (MOST)"** The meeting was jointly planned by NIDA DPMCDAs, the FDA, and the Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities

Networks (ACTION) public-private partnership with the FDA. It represented the second meeting of the ACTION Consortium for Addiction Research on Efficacy and Safety (CARES). The primary focus was to: 1) review past efforts in validating outcome measures for clinical trials in cocaine and methamphetamine dependence and 2) identify a research agenda for further efforts toward this goal.

GRANTEE HONORS AND AWARDS

Dr. Karl Deisseroth, D. H. Chen Professor of Bioengineering and of Psychiatry and Behavioral Sciences at Stanford University was awarded the Lurie Prize by the FNIH foundation.

Dr. Adam M. Leventhal, Associate Professor at the University of Southern California Keck School of Medicine, was awarded the Jarvik-Russell Early Career Award at the 2015 Society for Research on Nicotine and Tobacco meeting. This award, named after Murray Jarvik and Michael Russell, recognizes scientists early in their careers who have made extraordinary contributions to the field of nicotine and tobacco research.

STAFF HONORS AND AWARDS

Staff Honors and Awards

Dr. David Epstein, IRP, is co-chair of the Science Committee for the 2015 CEASE Baltimore tobacco-control research meeting.

Dr. Marilyn Huestis, IRP, received the Distinguished Fellow Award at the American Academy of Forensic Sciences (AAFS) annual meeting on February 18, 2015.

Dr. Marilyn Huestis received the Women Scientists Advisors 2015 NIDA Investigator Excellence in Research Award.

Dr. Richard Jenkins, DESPR, was appointed an Editorial Board member of American Journal of Community Psychology effective March 1, 2015.

Dr. Zuzana Justinova, IRP, received the NIDA Women Scientists Advisors Staff Scientist Award for her productive research career and mentoring of young scientists.

Dr. Yu (Woody) Lin, DCNBR, received the 2015 American Academy of Pain Medicine (AAPM) Presidential Commendations for bringing together the National Institutes of Health and the AAPM membership through a better understanding of NIH grant programs.

Dr. Samia Noursi, Women and Sex/Gender Differences Research Deputy Coordinator, DCNBR, joined, by invitation, the Editorial Board of Violence Research Digest: Translating Research into Policy and Practice. The Violence Research Digest is a new resource created by the National Partnership to End Interpersonal Violence (NPEIV; www.NPEIV.org), in particular its action team "Translation and Dissemination." The overarching mission of this team is to facilitate communication among researchers, policy makers, service providers and practitioners, in such a way that treatment and policy making is informed by research, and researchers are responsive to input from the field.

Dr. Karran Phillips, IRP, was selected to be the Special Symposia Chair for the Society of General Internal Medicine, 2015.

Dr. Rao Rapaka, DBNBR, was selected to receive the "2015 OXFORD International Society for Science of Botanicals (ICSB), Distinguished Achievement Award." He was cited for creativity, leadership and his contributions to promoting research on natural products' chemistry, herbals and designer drugs. The award will be presented at the 15th International conference on April 13, 2015.

Dr. John Satterlee, DBNBR, is the program lead for RFA-RM-14-008 Study of Nuclear Bodies and Compartments (U01), a new initiative of the Common Fund 4D Nucleome Program.

Dr. Yavin Shaham, IRP, accepted an offer to serve as an Associate (Handling) Editor at Neuropsychopharmacology (the official journal of the ACNP organization).

Dr. Elliot Stein, IRP, was appointed to the Advisory Boards of the Charleston Alcohol Research Center, Medical University of South Carolina, and the Translational Neuroimaging Analysis Center, Wake Forest School of Medicine.

Dr. Brandon Warren, IRP, received a \$2000 IBRO Travel award.

Dr. Cora Lee Wetherington was profiled by the Office of NIH History and Stetten Museum's social media for Women's History Month, March 2015. Social media included Twitter, Pinterest, Facebook, and Tumblr.

Drs. Comfort Boateng and **Rachel Slack**, IRP, were recipients of travel awards for the Behavior, Biology, and Chemistry: Translational Research in Addiction Meeting, in San Antonio, TX and presented talks at that meeting.

STAFF CHANGES

New Employees

Kristen Huntley, Ph.D. joined NIDA's Center for Clinical Trials Network (CCTN) group as a Health Scientist Administrator on March 8, 2015. She came to CCTN from the National Center for Complementary and Integrative Health (NCCIH) where she administered a portfolio of grants focused on the mechanisms of action, efficacy, and effectiveness of complementary health practices used for pain and symptom management in medical and mental health conditions. She led NCCIH efforts to build collaborations with other federal agencies, including the military and veteran populations. She has been most instrumental in facilitating the convening of an NCCIH Council Working Group to make recommendations to NCCIH regarding strengthening research collaborations, and conducting embedded research in clinical care in VA and DoD health care systems leveraging resources and use of medical record data. Previously, Dr. Huntley served as a scientific review officer at NIDA. Before that, she was on the faculty of Case Western Reserve University School of Medicine, Department of Pediatrics and worked as a project manager at Hauser and Associates, Inc., a market research firm in Paramus, New Jersey. Dr. Huntley received a BS in psychology from The University of Texas at Austin, and an M.S. and Ph.D. in clinical psychology from Texas A&M University.

Vani Pariyadath, Ph.D. joined DCNBR as a Program Officer in the Clinical Neuroscience Branch on March 23, 2015. Vani received her Bachelor's degree in Computer Science in 2003, from the University of Pune, and a Master's degree in Cognitive Science in 2005, from the University of Allahabad, both in India. She then joined Dr. David Eagleman's lab in Houston, Texas to begin doctoral research on time perception. Her graduate work investigated the neural underpinnings of time perception, specifically through understanding how duration perception and its underlying neurocircuitry are shaped by novelty and predictability. In the spring of 2010, after receiving a Ph.D. in Neuroscience from Baylor College of Medicine (Houston, Texas), Vani joined the Neuroimaging Research Branch at the NIDA-IRP to carry out postdoctoral research under Dr. Elliot Stein's mentorship. Her work here focused on understanding vulnerability to drug addiction using behavioral measures combined with multiple MRI techniques. Vani's primary research investigated individual differences in reward and punishment learning, and how these differences are shaped by childhood adversity and how they might influence the risk for nicotine addiction. In addition, she was involved in a project examining the acute effects of MDMA (ecstasy) administration, and in another that applied machine learning approaches to identify neural features predictive of smoking status. Vani's areas of scientific interest and expertise include the cognitive neuroscience of decision-making, risk factors for drug addiction, reward and reinforcement circuits, time perception, and the application of big analytical methods to brain imaging. Her interests are in using behavioral measures and neuroimaging to address questions in these areas.

Destiny Aighe joined NIDA's OM/OA NIDA R&D Branch as a Contract Specialist on April 19, 2015. Destiny comes to NIDA from the private sector.

Gary Berkson joined NIDA's OM/OA NIDA R&D Branch as a Contract Specialist on April 19, 2015. Gary comes to NIDA from the private sector.

Daniel Collector joined the IRP's Molecular Neuropsychiatry Research Branch as a post-baccalaureate IRTA in January 2015.

Arthur Godino, a graduate student from the Ecole Normale Supérieure de Lyon, France is being trained to conduct epigenetic studies under the supervision of Drs. Oscar Torres and Subramaniam Jayanthi in the Molecular Neuropsychiatry Research Branch. He is pursuing a master's degree in Biology in Lyon and will apply these techniques when he returns to France.

Jacqueline Keighron, Ph.D., has joined the IRP's Medication Development Program as a post-doctoral fellow. Dr. Keighron will be involved in research projects about the functional characterization of different afferent inputs to the ventral tegmental area using optogenetic and voltammetry procedures.

Keshia McDonald joined NIDA's OM/OA Station Support Branch as a Contract Specialist on April 19, 2015. Keshia comes to NIDA from the private sector.

Christopher Weaver joined NIDA's OM/OA NIDA R&D Branch as a Contract Specialist on April 19, 2015. Christopher comes to NIDA from the private sector.

Departures

Dr. Eve Reider of DESPR's Prevention Research Branch accepted a position at the National Center for Complementary and Integrative Health (NCCIH) (formerly NCCAM) in March 2015. During her 15 year tenure at NIDA, Eve focused her efforts on the goals of advancing prevention science and improving public health. At NCCIH, she will be leading their military/veteran initiative and expanding their prevention/health promotion portfolio.

Dr. George Uhl, IRP, accepted a position as Associate Chief of Staff for Research at the New Mexico VA Health care system, and President of the Biomedical Research Foundation of New Mexico. He became a Guest Researcher at, and will continue to lead under the direction of J-L Cadet, the NIDA Molecular Neurobiology Research laboratory, which is becoming a section in Dr. Cadet's Molecular Neuropsychiatry Research Branch at the NIDA IRP.

Debasis Goswami, an Information Technology Specialist in the Office of Management's Information and Resource Management Branch left NIDA on March 3, 2015 for a position at NHLBI.

Patrick Kenney, a Contract Specialist in the OM/OA NIDA R&D Branch, left NIDA on March 21, 2015, for a position with the Veteran's Administration.

Shaun Miles, a Contract Specialist in the OM/OA Station Support Branch left NIDA on February 21, 2015, for a position with the Department of the Navy.

Retirements

David (Davey) Jones, a loyal and dedicated Mail and File Clerk in the Office of Management's Administrative Management and Analysis Branch retired from Federal Service on April 3, 2015 after 45 years of outstanding service to NIDA.

Harriette Jordan, a Secretary in the Office of Management's Administrative Management and Analysis Branch who has made substantial contributions to NIDA's mission and served in variety of key roles during her 20 year tenure, retired on April 3, 2015 after 35 years of Federal Service.



National Institute
on Drug Abuse